

-



wherein x is 1, 2, 3 or 4; m is 1 or 2; n is 1 or 2;

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Z is 0 or a bond;

X is CH or N;

substituted amino;

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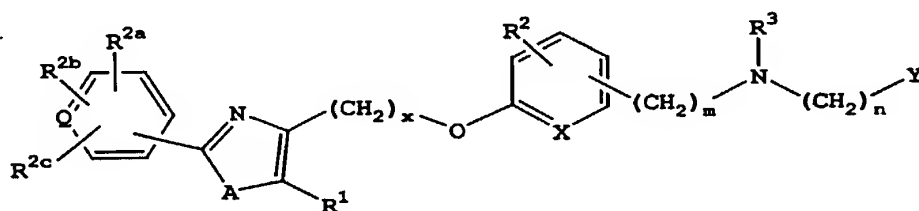
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haloalkoxyaryloxy carbonyl, alkoxycarbonylaryloxy carbonyl,
 aryloxyaryloxy carbonyl, arylsulfinylaryl carbonyl,
 arylthioaryl carbonyl, alkoxycarbonylaryloxy carbonyl,
 arylalkenyloxy carbonyl, heteroaryloxyarylalkyl,
 5 aryloxyaryl carbonyl, aryloxyarylalkyloxy carbonyl,
 arylalkenyloxy carbonyl, arylalkyl carbonyl,
 aryloxyalkyloxy carbonyl arylalkylsulfonyl,
 arylthiocarbonyl, arylalkenylsulfonyl,
 heteroarylsulfonyl, arylsulfonyl, alkoxylarylalkyl,
 10 heteroarylalkoxy carbonyl, arylheteroarylalkyl,
 alkoxylaryl carbonyl, aryloxyheteroarylalkyl,
 heteroarylalkyloxyarylalkyl, arylarylalkyl,
 arylalkenylarylalkyl, arylalkoxyarylalkyl,
 arylcarbonylarylalkyl, alkylaryloxyarylalkyl,
 15 arylalkoxy carbonyl heteroarylalkyl, heteroarylarylalkyl,
 arylcarbonyl heteroarylalkyl, heteroaryloxyarylalkyl,
 arylalkenyl heteroarylalkyl, arylaminoarylalkyl or
 aminocarbonylarylalkyl;

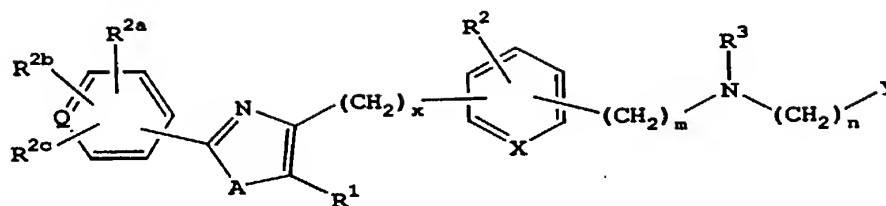
Y is CO_2R^4 (where R^4 is H or alkyl, or a prodrug
 20 ester) or Y is a C-linked 1-tetrazole, a phosphinic acid
 of the structure $\text{P}(\text{O})(\text{OR}^{4a})\text{R}^5$, (where R^{4a} is H or a prodrug
 ester, R^5 is alkyl or aryl) or a phosphonic acid of the
 structure $\text{P}(\text{O})(\text{OR}^{4a})_2$, (where R^{4a} is H or a prodrug ester);

including all stereoisomers thereof, prodrug
 25 esters thereof, and pharmaceutically acceptable salts
 thereof, with the proviso that where X is CH, A is O, Q
 is C, Z is O and Y is CO_2R^4 , then R^3 is other than H or
 alkyl containing 1 to 5 carbons in the normal chain.

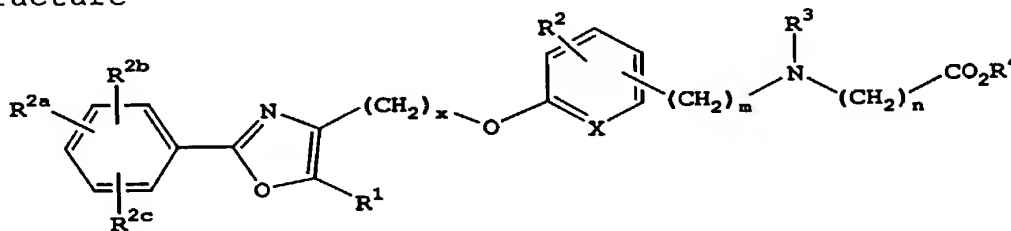
30 2. A compound having the structure



or

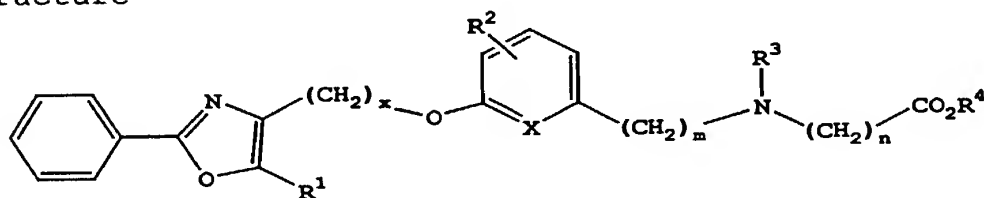


3. The compound as defined in Claim 1 having the structure



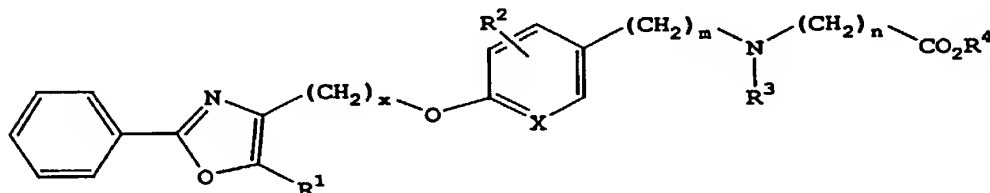
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4. The compound as defined in Claim 1 having structure



or

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5. The compound as defined in Claim 1 wherein $(CH_2)_x$ is alkylene, alkenylene, allenyl, or alkynylene.

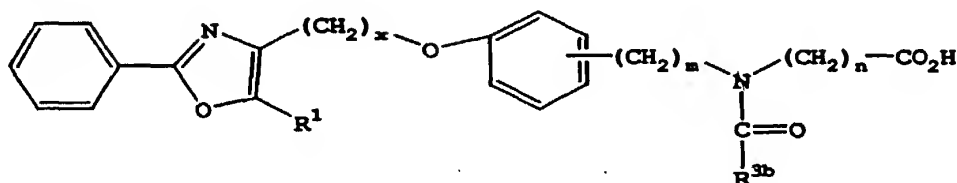
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6. The compound as defined in Claim 4 wherein X is CH.

7. The compound as defined in Claim 4 wherein X is N.

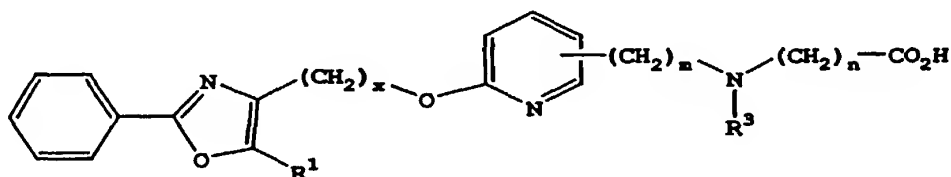
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8. The compound as defined in Claim 1 having the structure



wherein R^1 is alkyl, R^{3b} is arylalkylamino, aryl-
 5 arylamino, arylamino, alkoxyarylamino, dialkoxyarylamino, dihaloarylamino or alkylthioarylamino.

9. The compound as defined in Claim 1 having the structure



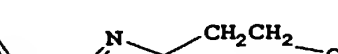
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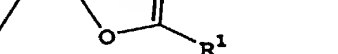
10. The compound as defined in Claim 1 wherein R^{2a} is alkoxy or H,


(CH_2)_x is CH_2 , (CH_2)₂, (CH_2)₃, or $\begin{array}{c} CH_3 \quad CH_3 \\ \diagdown \quad / \\ C \\ / \end{array}$, (CH_2)_m is CH_2 , or
 15 $\begin{array}{c} R^a \\ | \\ -CH- \end{array}$ (where R^a is alkyl or alkenyl), (CH_2)_n is CH_2 , R^1 is lower alkyl, preferably $-CH_3$, R^2 is H, R^{2a} is H, R^4 is H, X is CH, and R^3 is arylalkyloxycarbonyl, arylheteroarylalkyl, aryloxyarylalkyl, arylalkyl, aryloxycarbonyl, haloaryl-oxycarbonyl,
 20 alkoxyaryloxycarbonyl, alkylaryloxycarbonyl, aryloxyaryloxycarbonyl, heteroaryloxycarbonyl, aryloxyarylcarbonyl, arylalkenyloxycarbonyl, cycloalkylaryloxycarbonyl, arylalkylarylcarbonyl, heteroaryl-heteroarylalkyl,
 25 cycloalkyloxyaryloxycarbonyl, heteroaryl-heteroarylcarbonyl, alkyloxyaryloxycarbonyl, arylalkylsulfonyl, arylalkenylsulfonyl, alkoxyarylalkyl, arylthiocarbonyl, cycloheteroalkylalkyloxycarbonyl, cycloheteroalkyloxycarbonyl, or polyhaloalkylaryloxy-
 30 carbonyl, which may be optionally substituted.

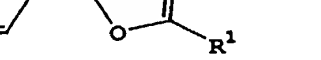
5 12. The compound as defined in Claim 5 wherein X
is N.

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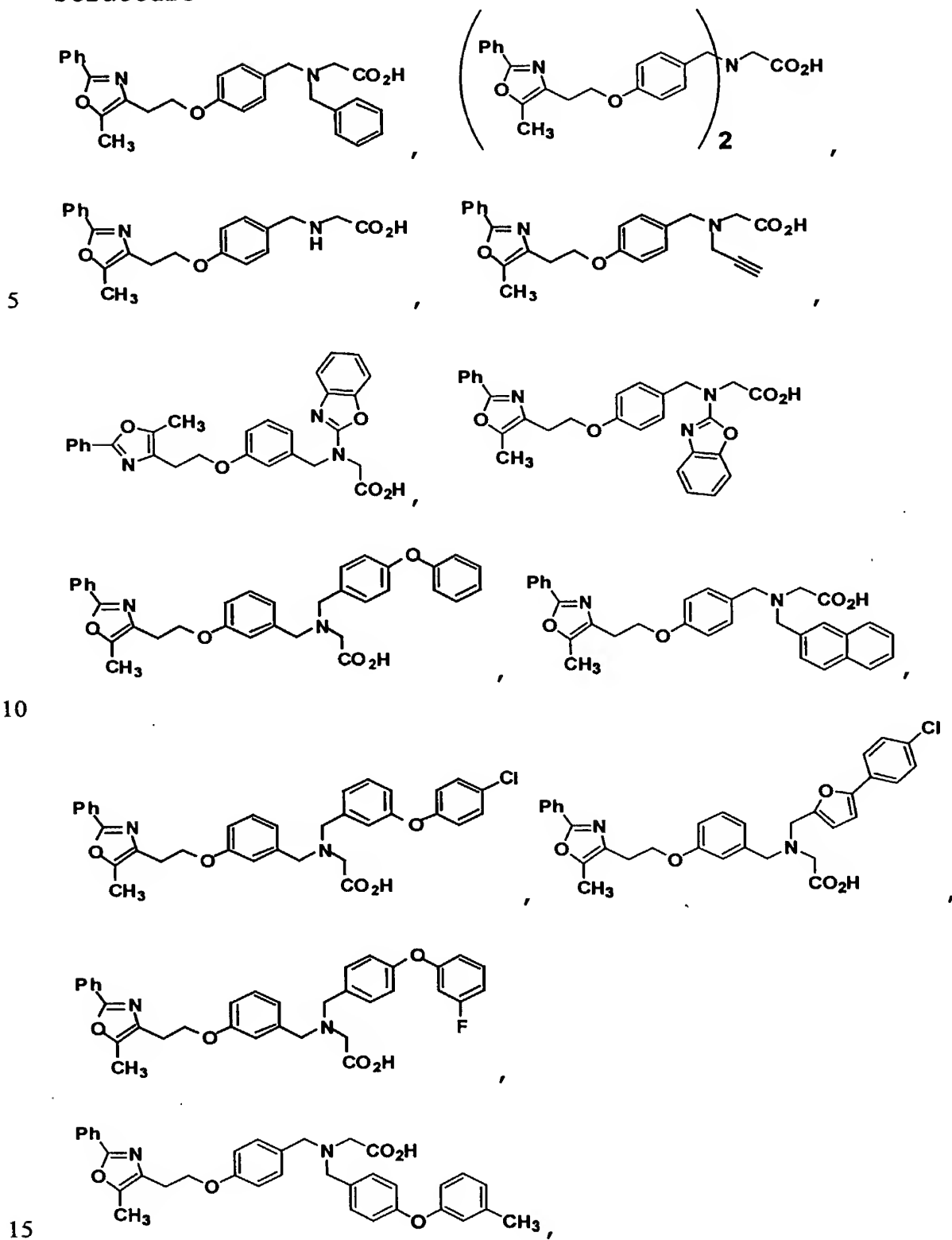
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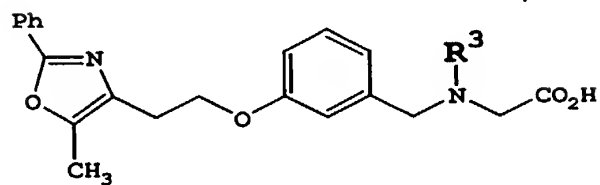
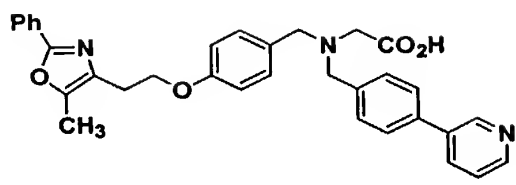


 or
 

where $(\text{CH}_2)_n$ is CH_2 or $\begin{array}{c} \text{CH}_3 \\ | \\ \text{---CH---} \end{array}$.

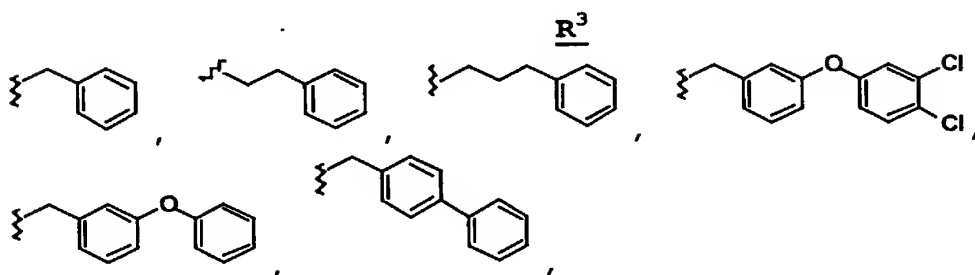
16. The compound as defined in Claim 1 having the structure



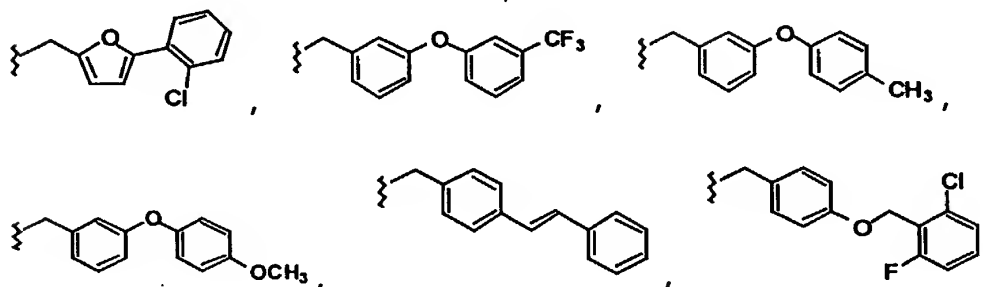


, where $R^3 =$

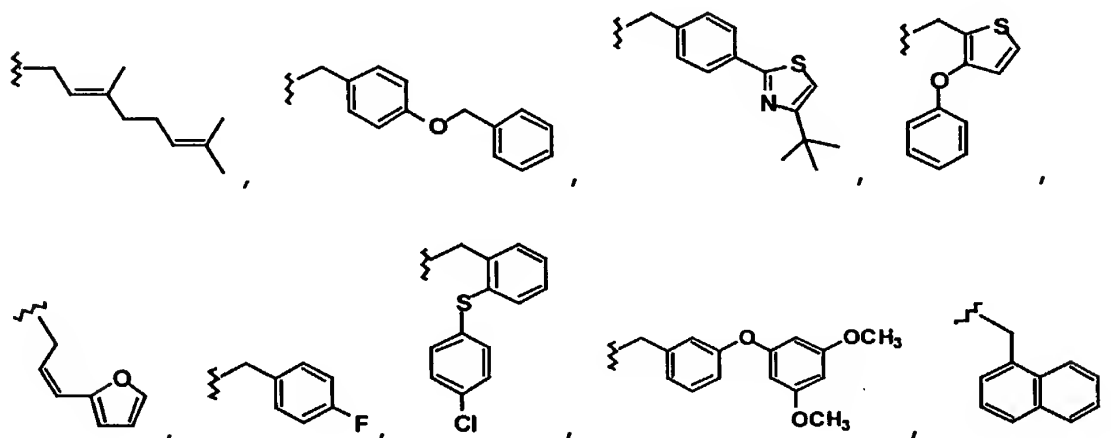
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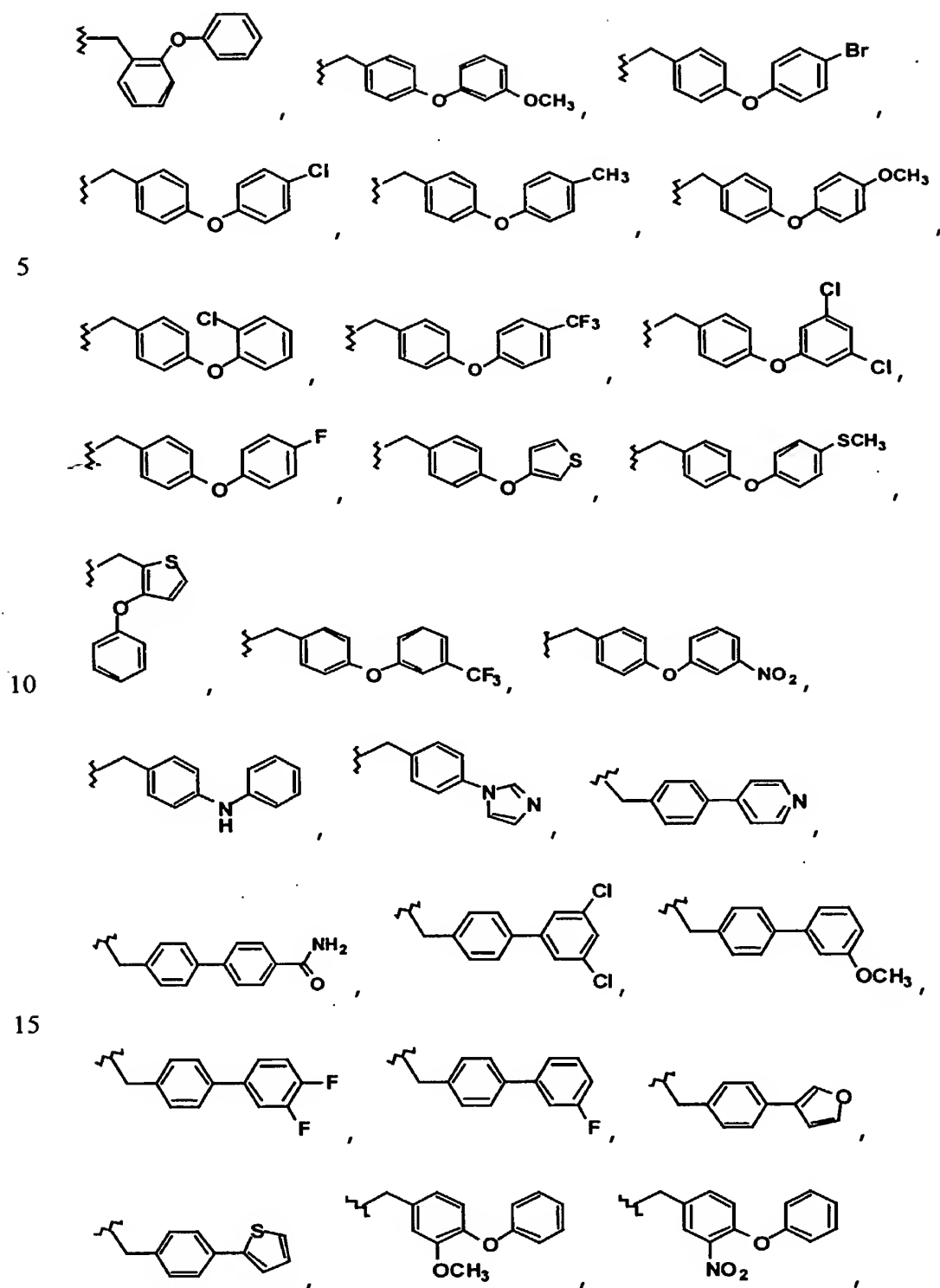


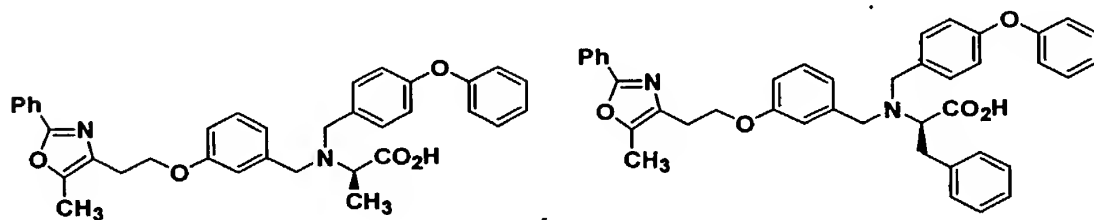
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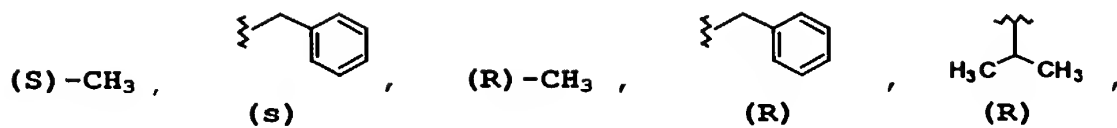
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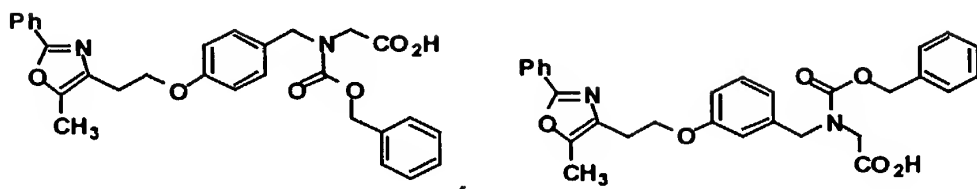
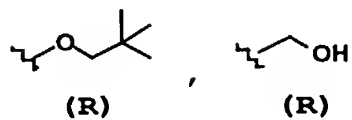




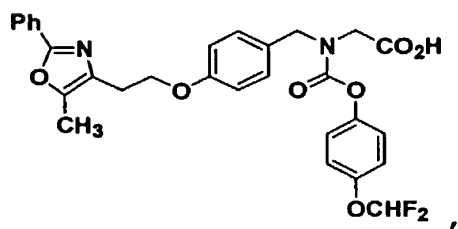
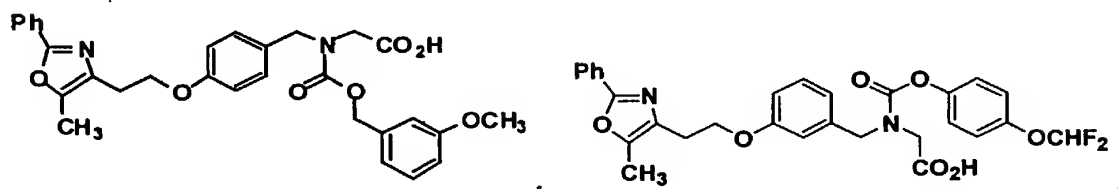
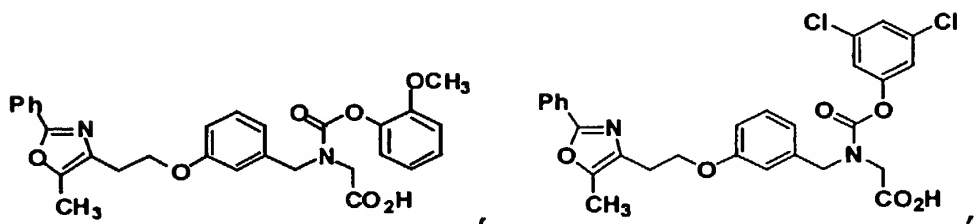
, where $R^{3c} =$



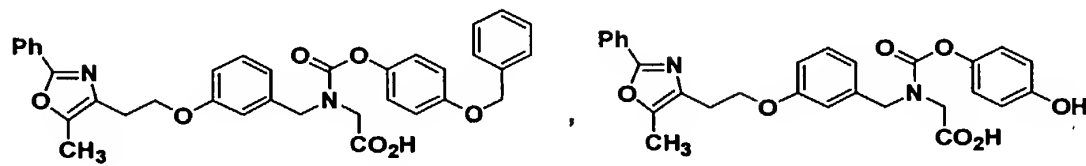
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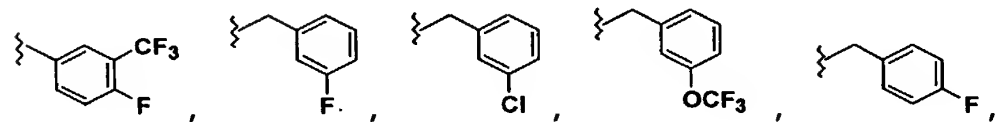


The figure displays 15 chemical structures of monomers used in the synthesis of poly(arylene ether)s, arranged in three rows. Each structure is preceded by a wavy line indicating its attachment point to a polymer chain. The monomers are:

- Row 1:
 - 2,2,2-trifluoroethyl 4-(2,3-dihydrobenzofuran-5-yl)acetate
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl trifluoromethyl ether
 - 1-(2,3-dihydrobenzofuran-5-yl)-4-(trifluoromethoxy)phenyl
- Row 2:
 - 1,2-dimethoxy-4-(2,3-dihydrobenzofuran-5-yl)benzene
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl methyl ether
 - 4-(2,3-dihydrobenzofuran-5-yl)-2-bromo-1-methylphenyl
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl methyl sulfide
- Row 3:
 - 4-(2,3-dihydrobenzofuran-5-yl)-2-chloro-1-methylphenyl
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl fluoride
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl chloride
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl bromide
 - 4-(2,3-dihydrobenzofuran-5-yl)phenyl trifluoromethyl ether

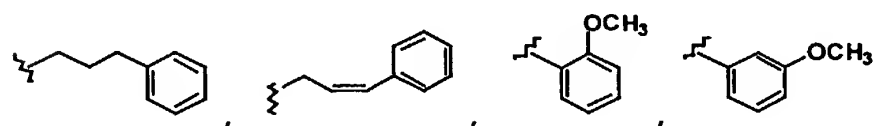
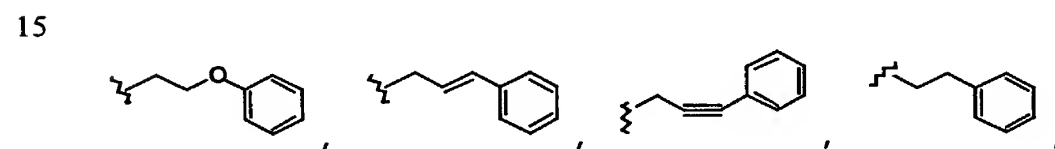
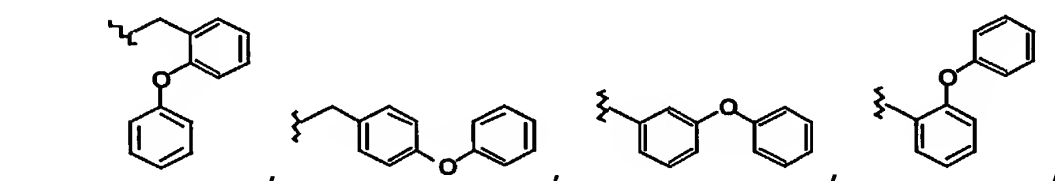
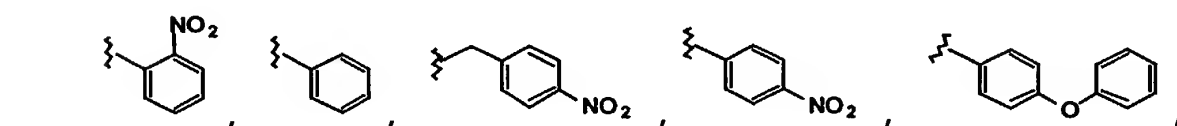
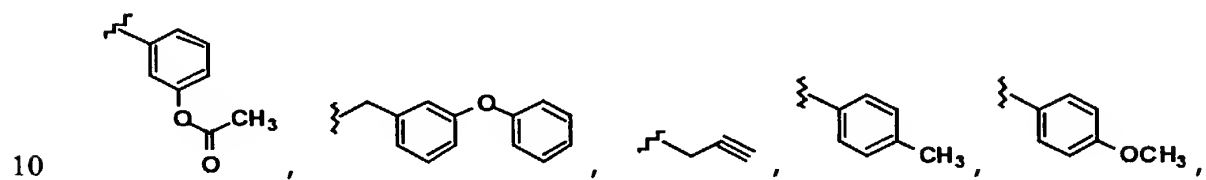
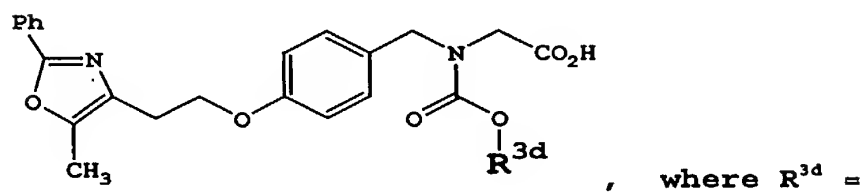
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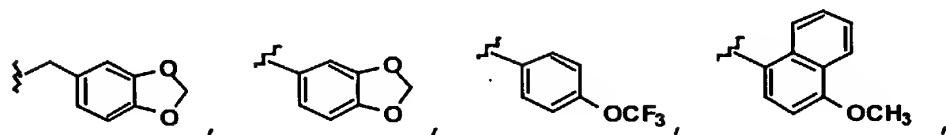
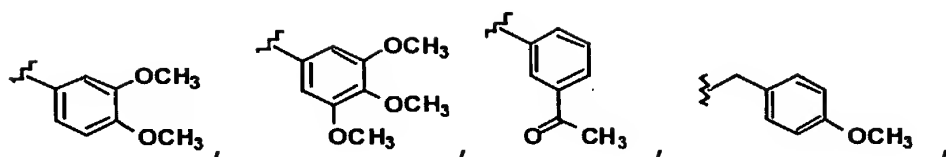
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*c1ccc(C(C)(C)C)cc1, *c1ccc(C(C)C)cc1, *c1ccc(CCc2ccccc2)cc1, *c1ccc(CC)cc1



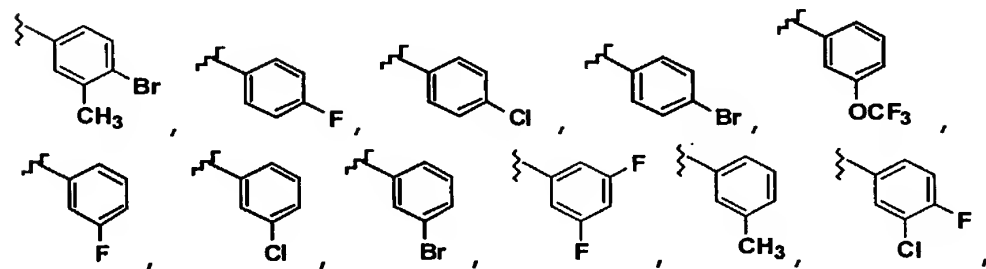
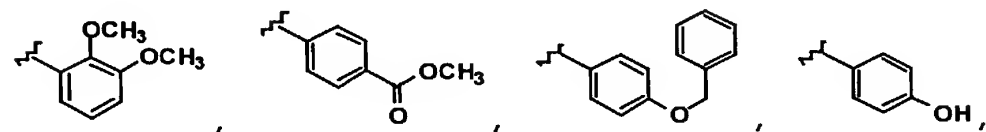
Chemical structures of the monomers used in the synthesis:

- 4-chlorobenzyl monomer: Clc1ccc(CO)cc1
- 4-(trifluoromethoxy)benzyl monomer: COc1ccc(CO)cc1
- 3,4-dimethoxybenzyl monomer: COc1cc(CO)cc(OC)c1

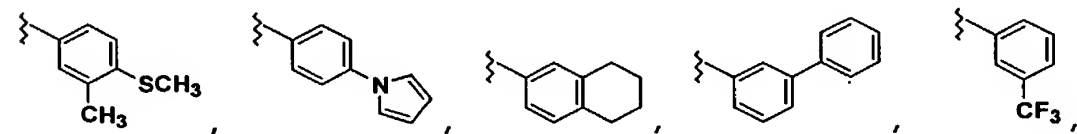
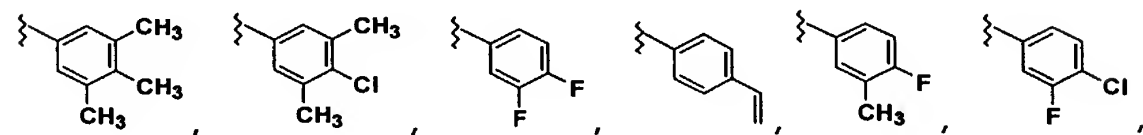




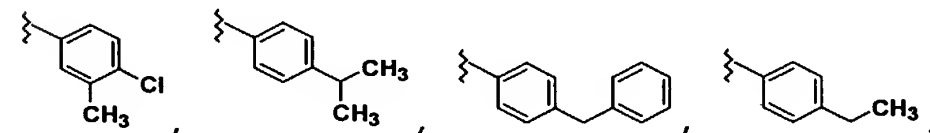
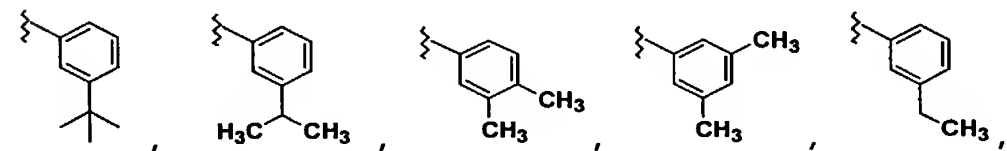
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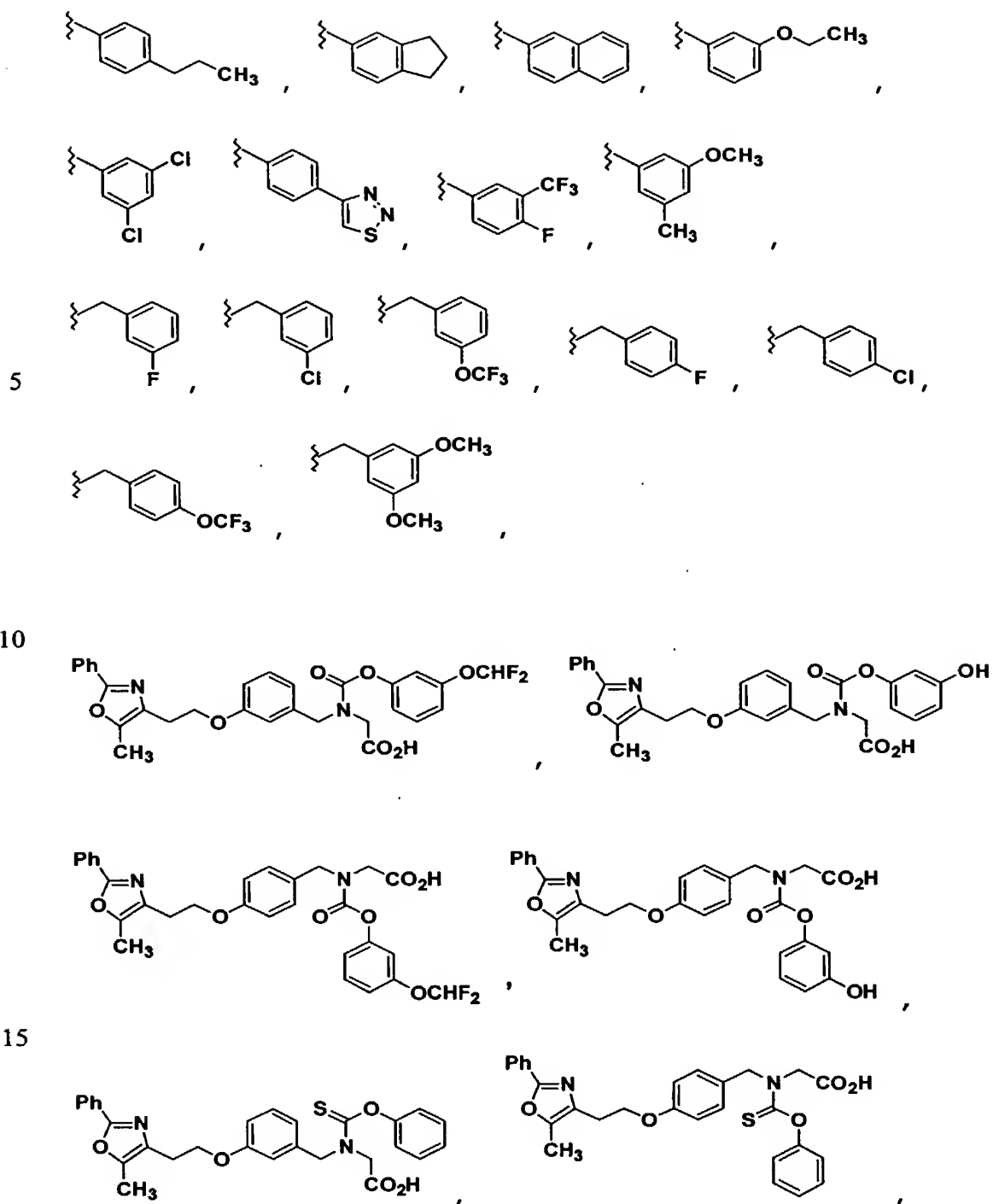


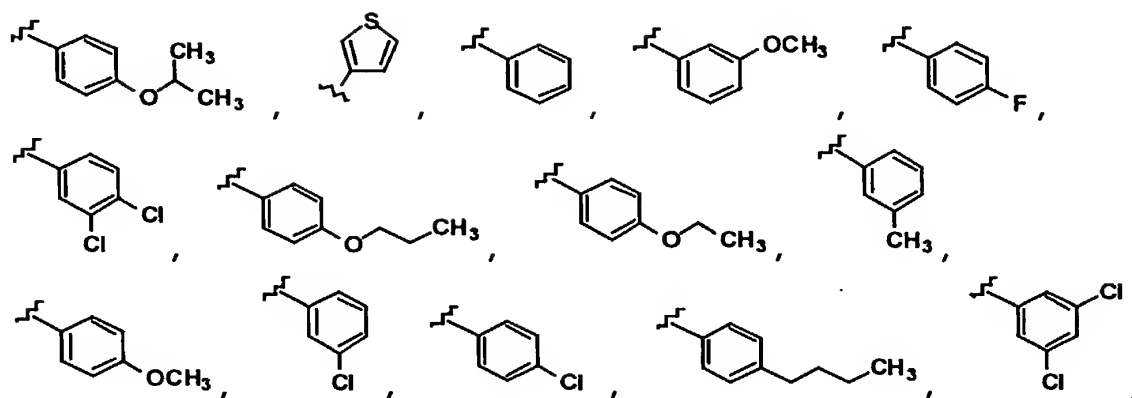
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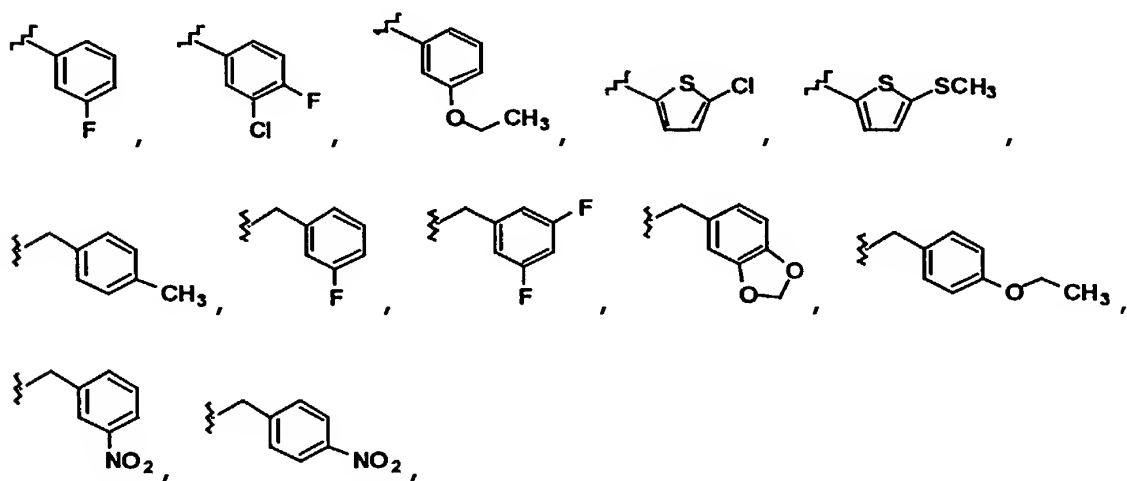
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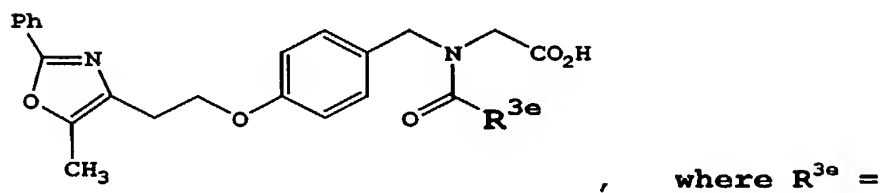




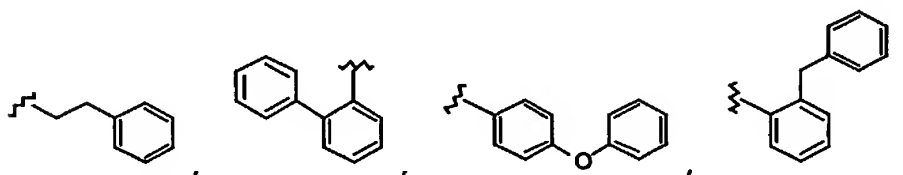
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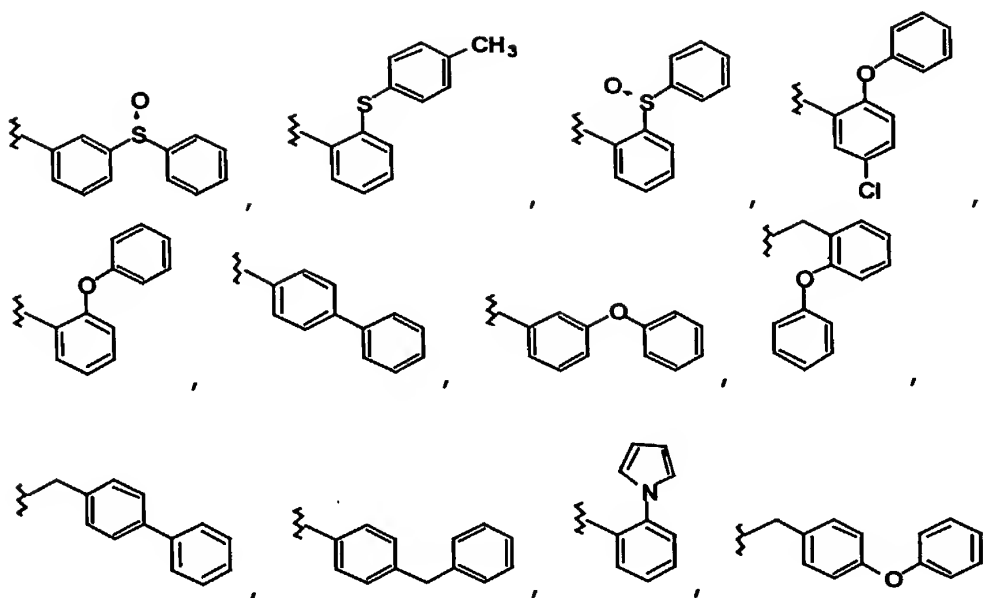


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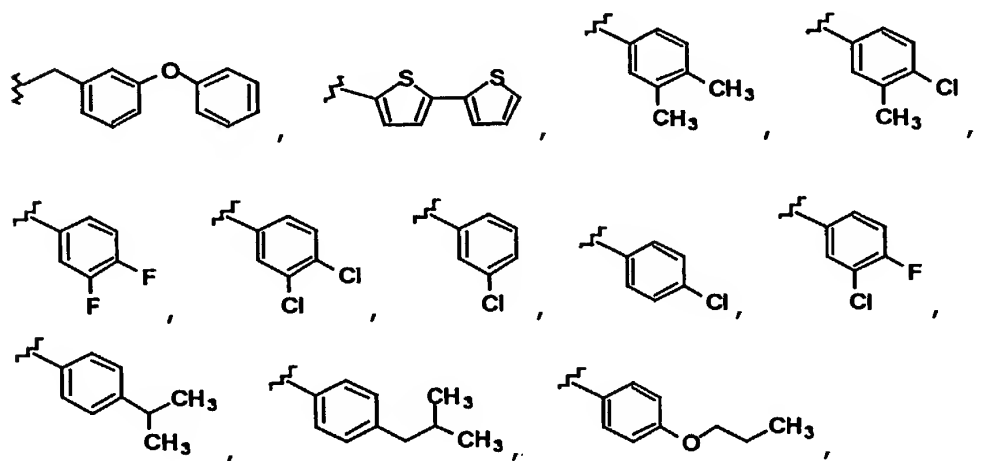


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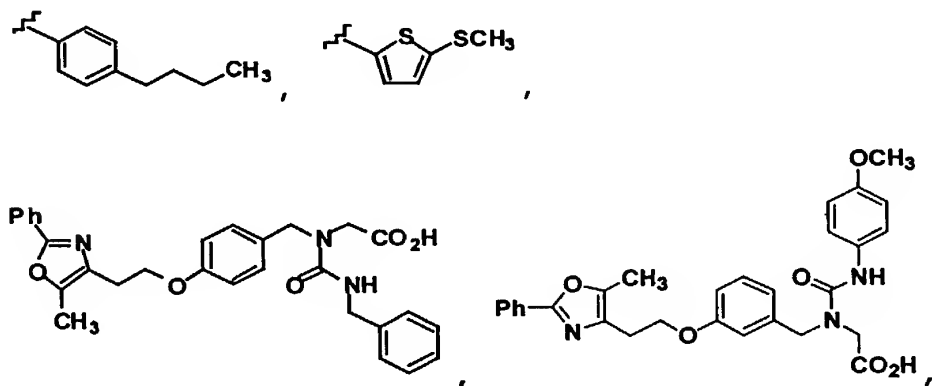


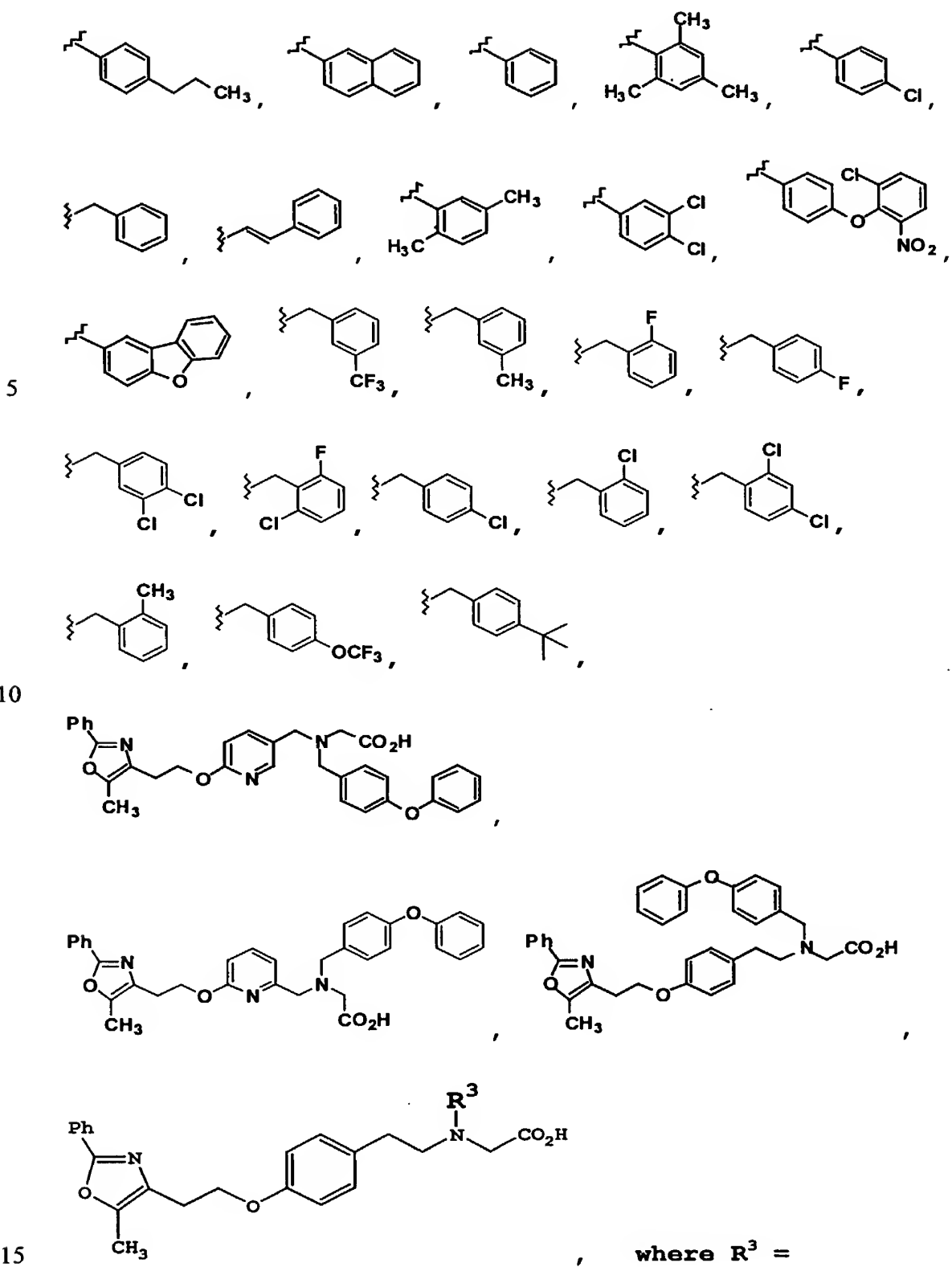


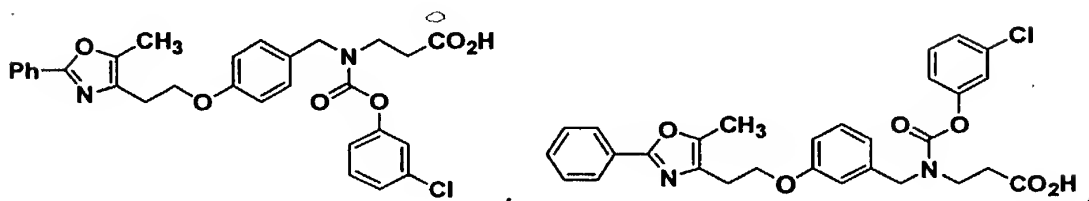
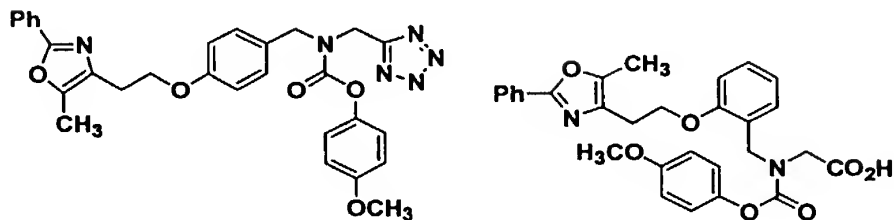
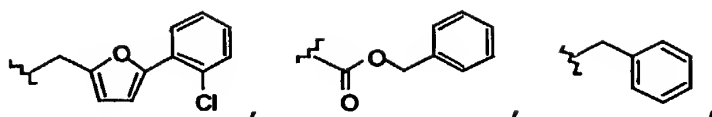
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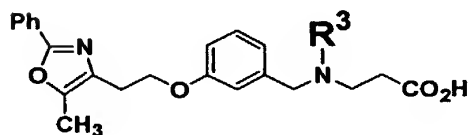
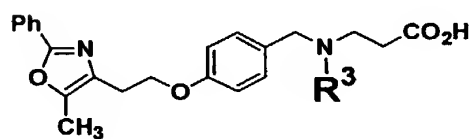
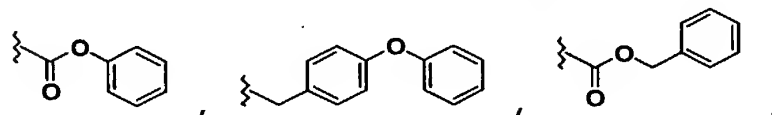
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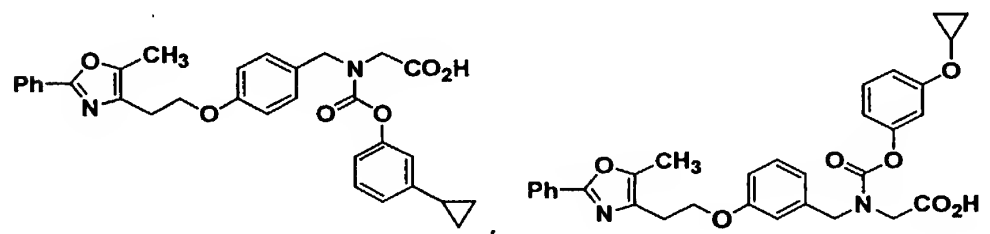
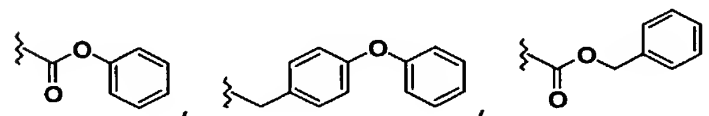




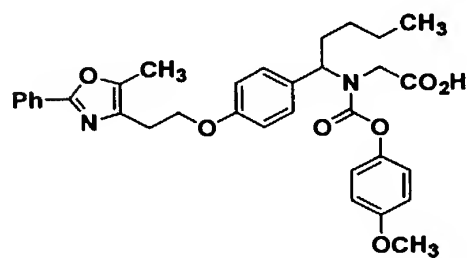
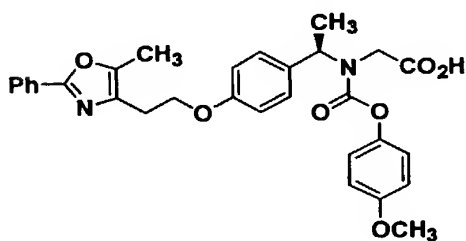
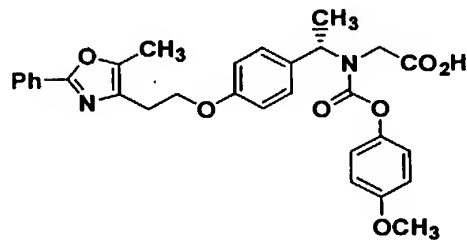
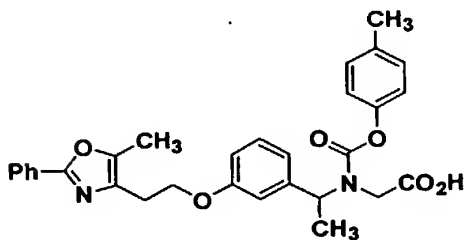
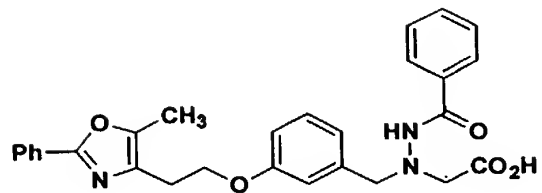
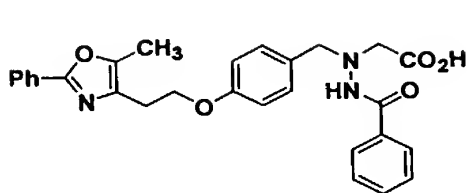
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where $R^3 =$ 

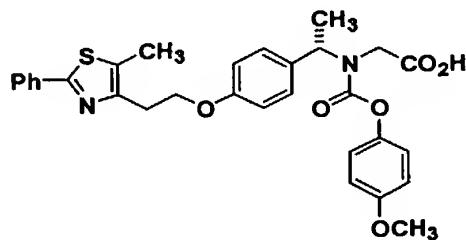
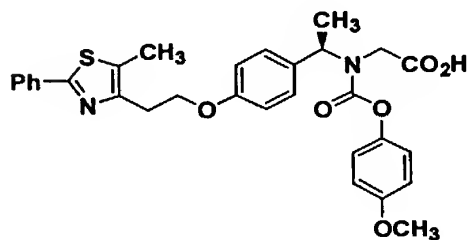
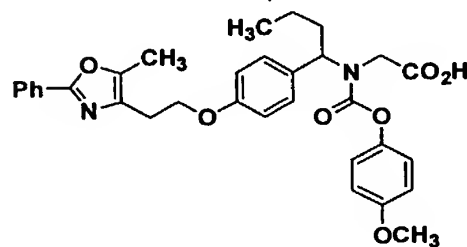
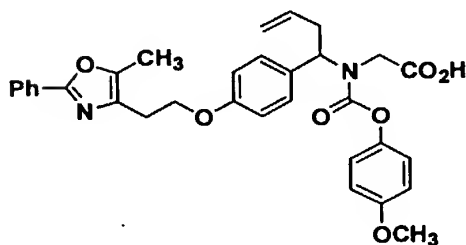
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, where $R^3 =$ 

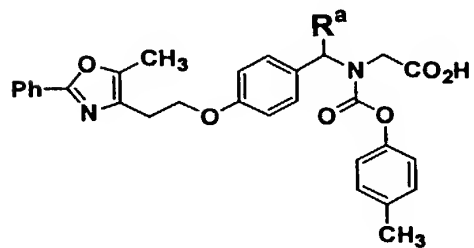
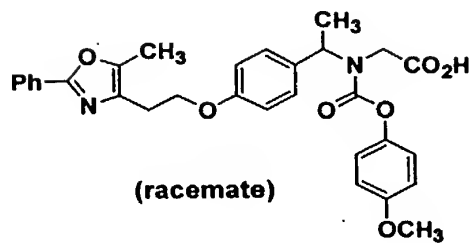
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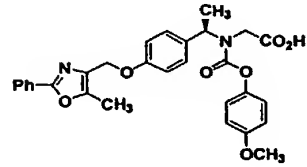
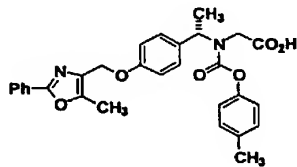
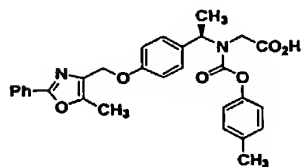
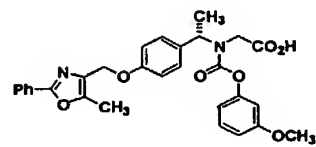
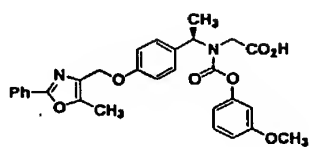
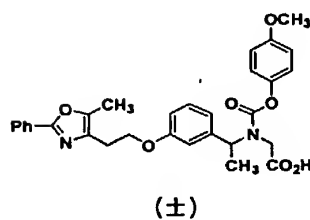
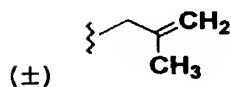
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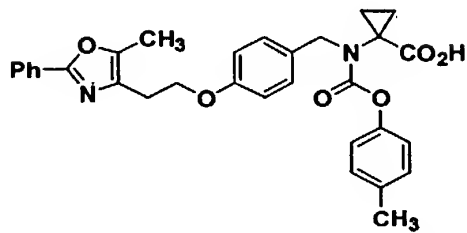
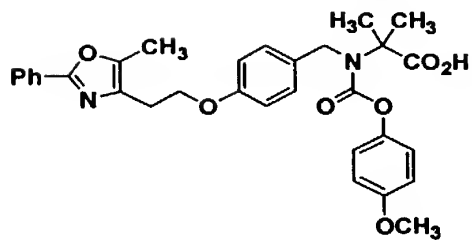
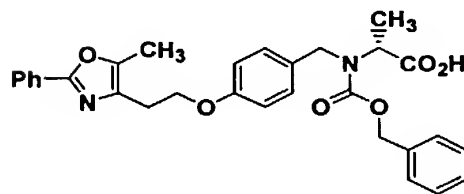
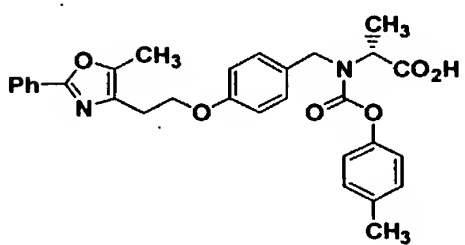
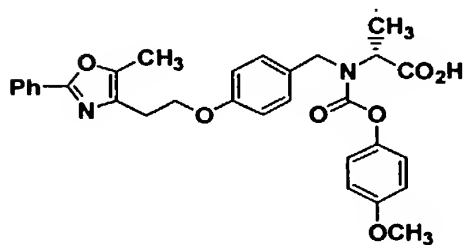
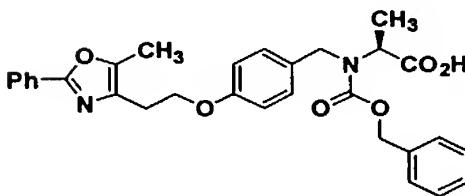


where $R^a = (\pm)\text{-Me}$, $(\pm)\text{ n-Bu}$,

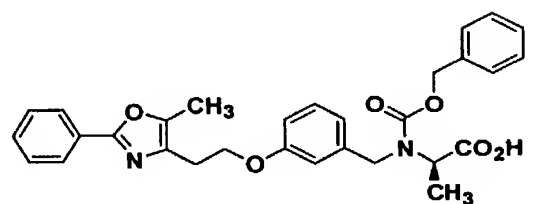
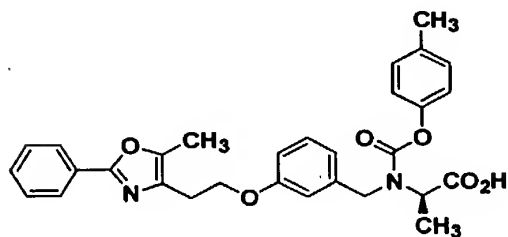
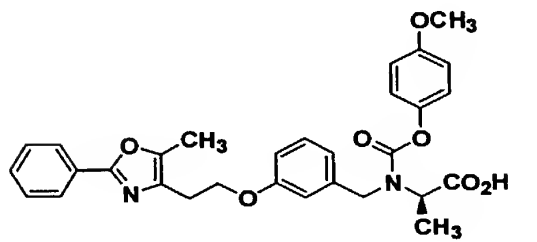
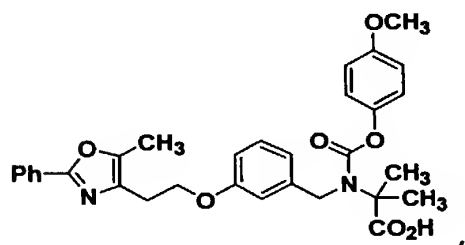
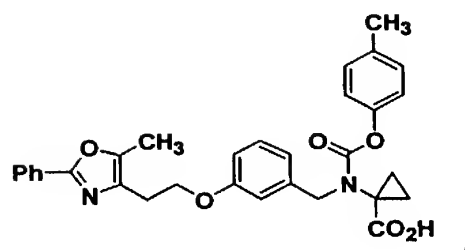
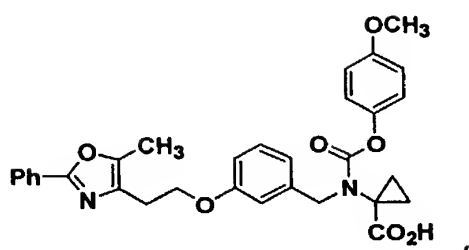
CC1=C(C(=O)OCC1c2ccccc2)c3cc(OC)ccc3OC(=O)N(C)C(R)c4ccc(OCC5=C(C)N=C(C6=CC=CC=C6)O5)cc4

where $R^a = (\pm) Et, (\pm) i-Bu,$

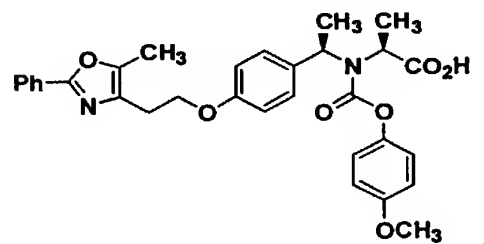
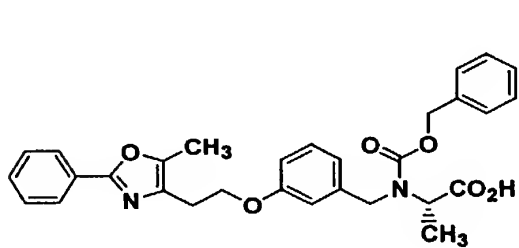
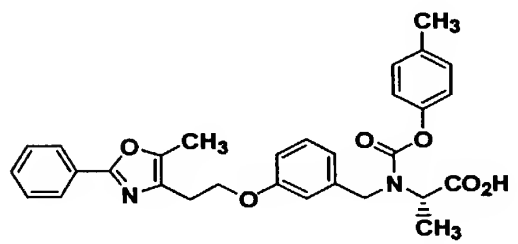
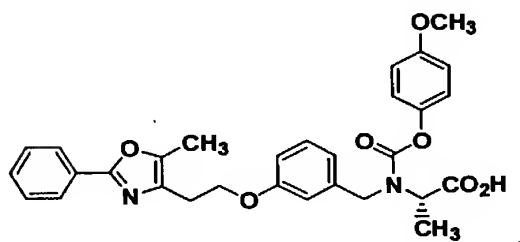


CC1=C(C(=O)O)N(C1C(=O)Oc2ccc(OC)cc2)Cc3ccc(OCCc4c(C)nc(C5=CC=CC=C5)c4)cc3

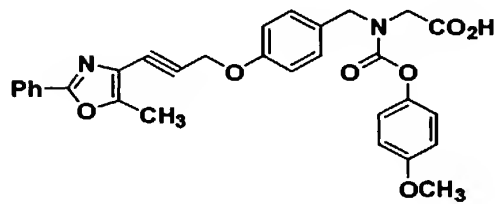
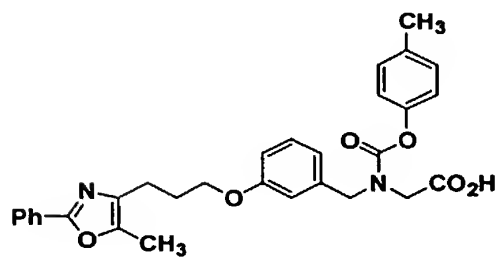
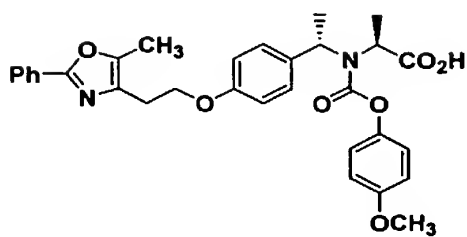
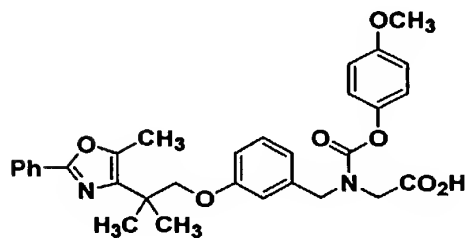
- 351 -



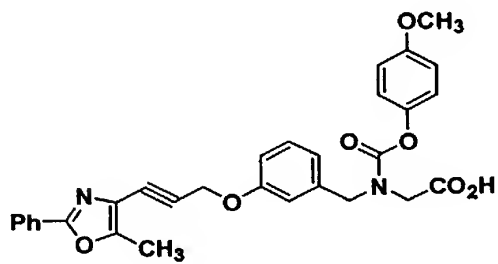
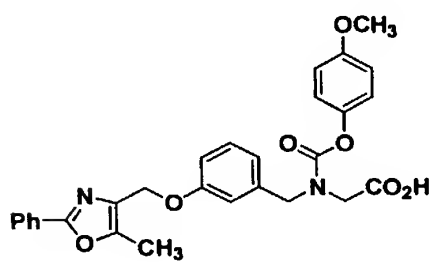
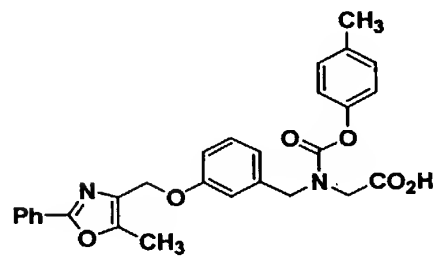
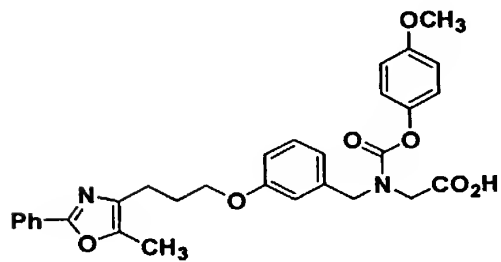
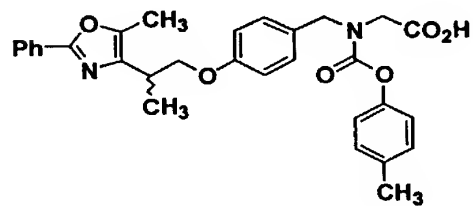
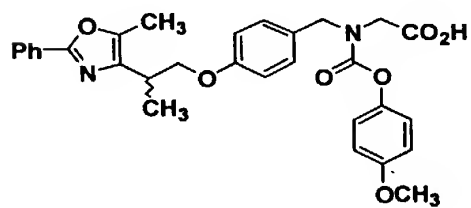
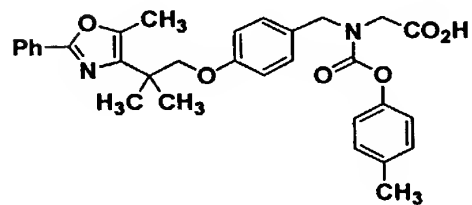
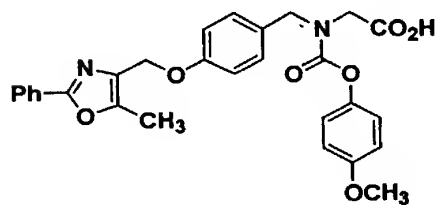
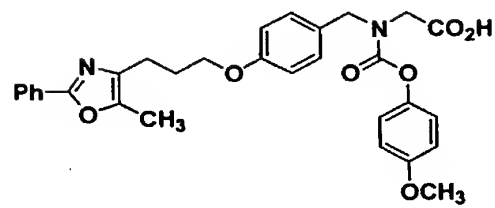
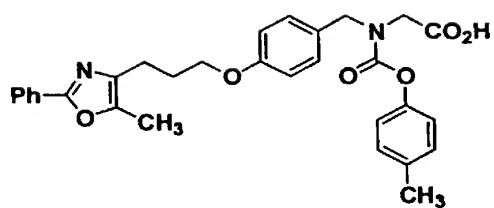
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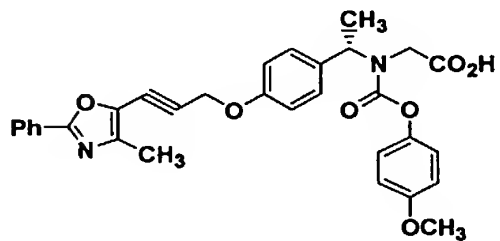
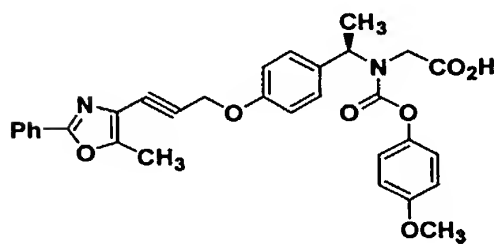
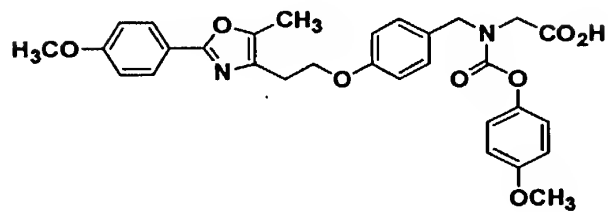
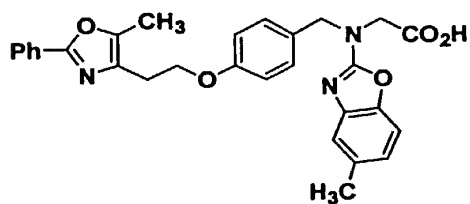
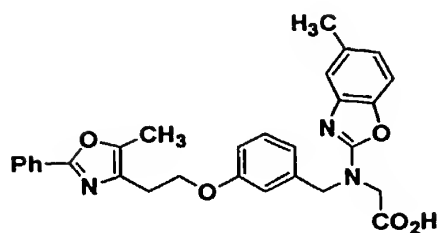
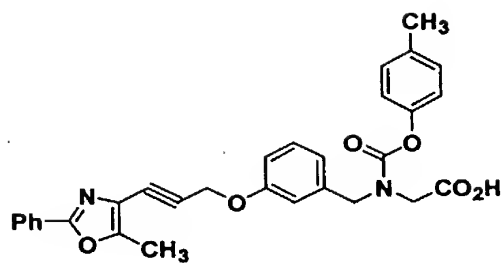
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COc1ccc(Oc2c(=O)nc(Cc3ccc(OCC4=CC=C(C=C4)C5=CC(=CN(C5)C6=CC=CC=C6)C=C6)C=C3)cc2)cc1

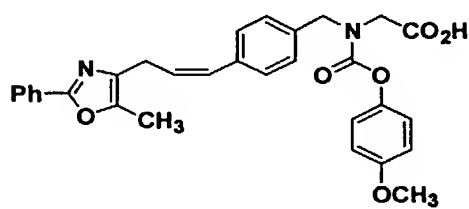
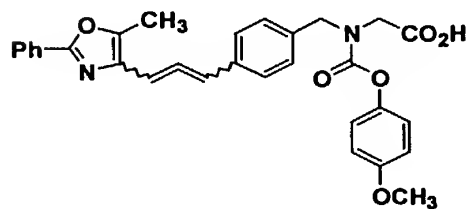
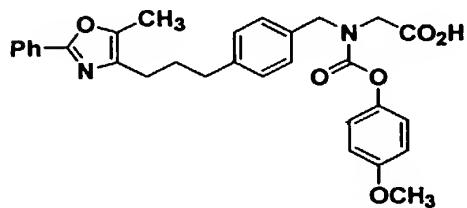
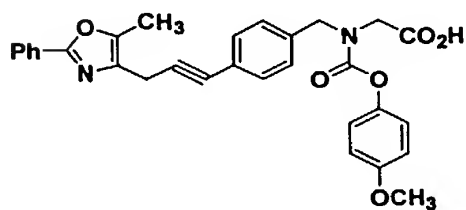
- 353 -



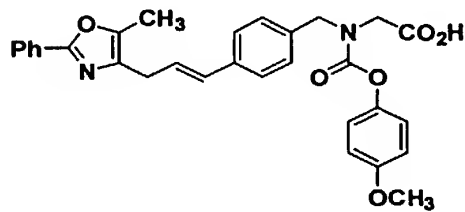
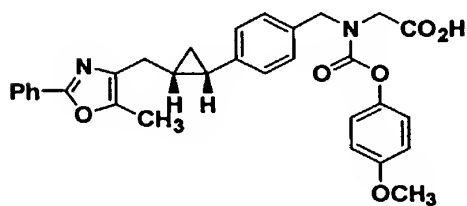
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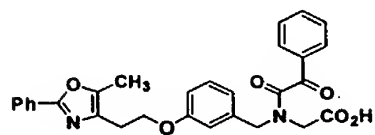
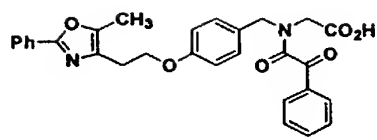
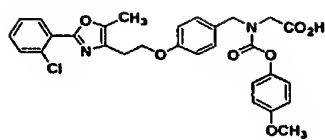


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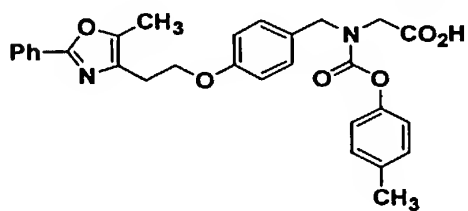
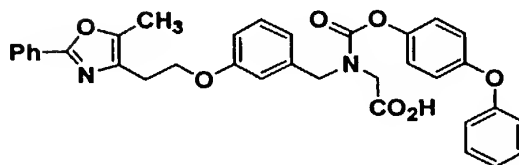
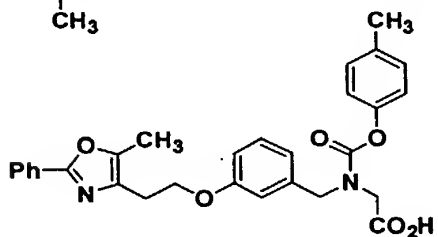
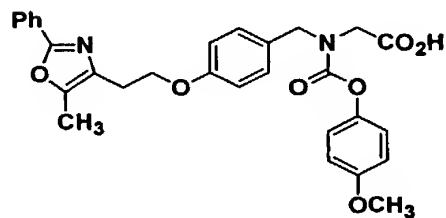
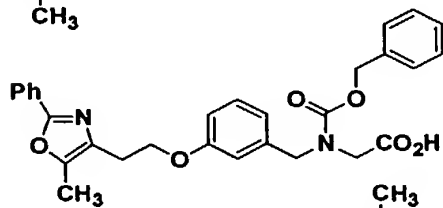
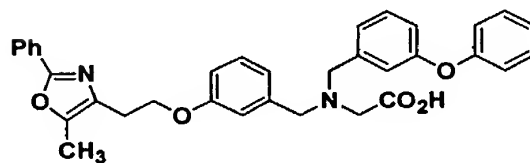
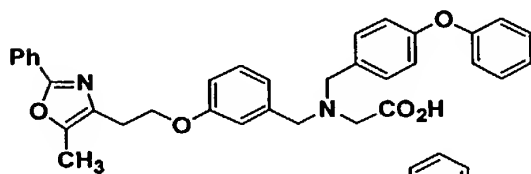
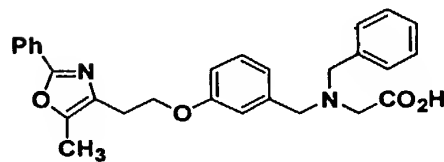
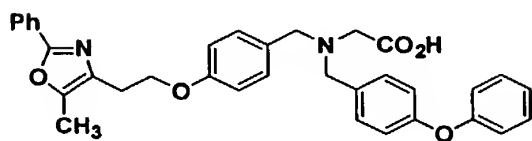
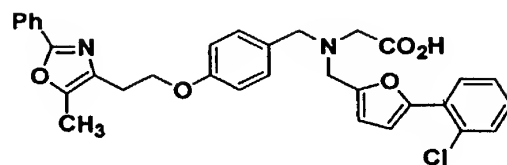
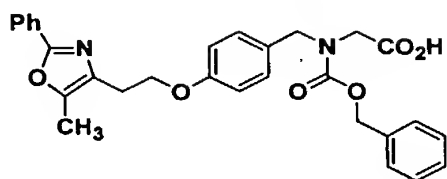
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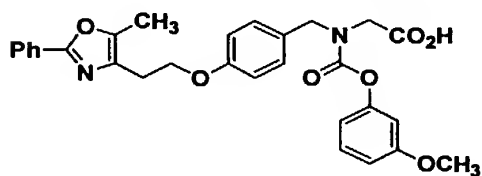
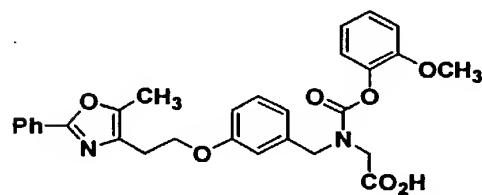
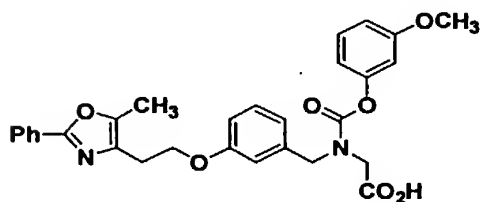
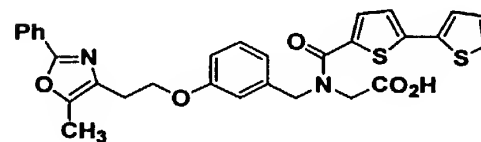
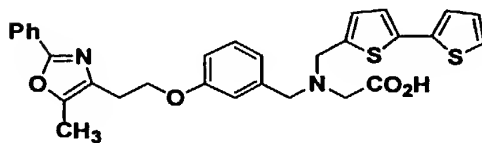
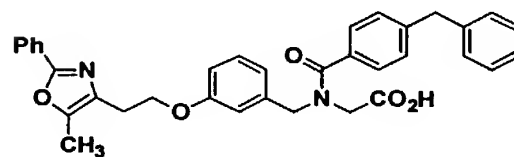
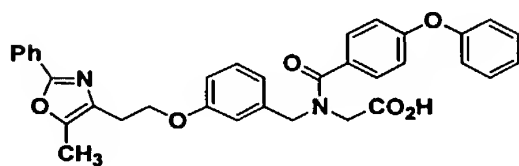
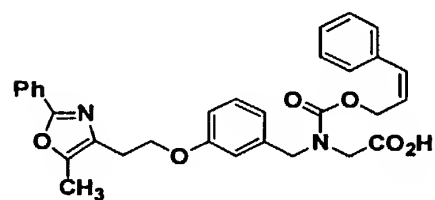
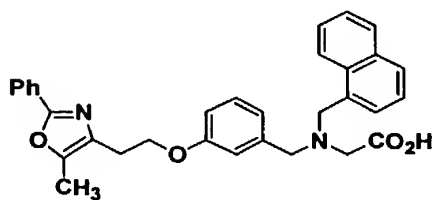
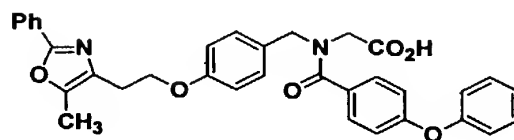
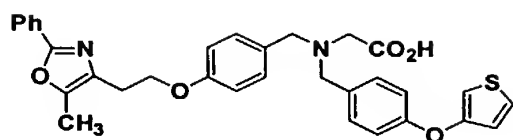


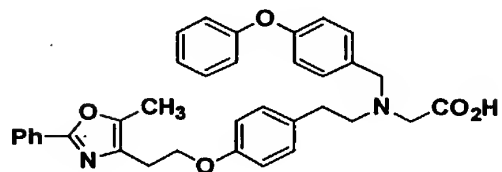


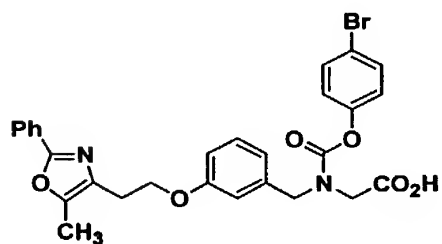
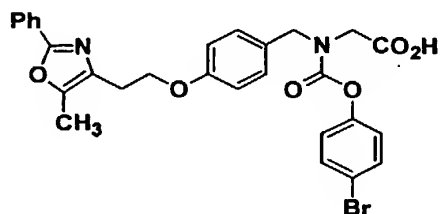
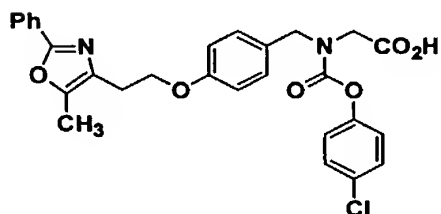
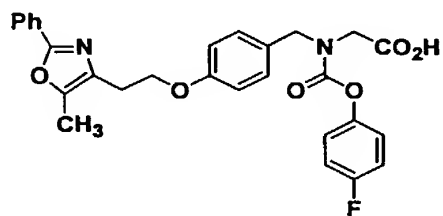
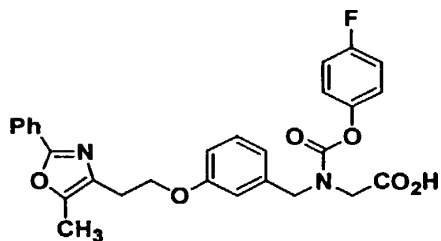
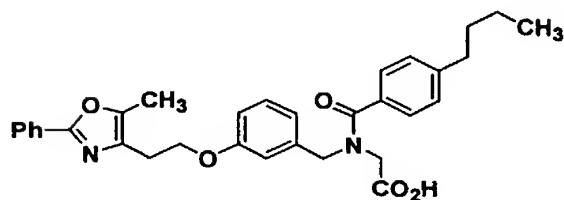
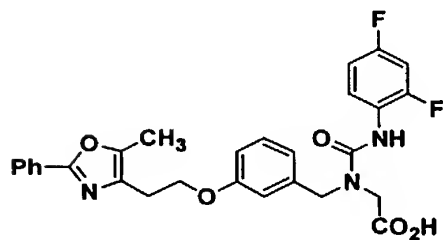
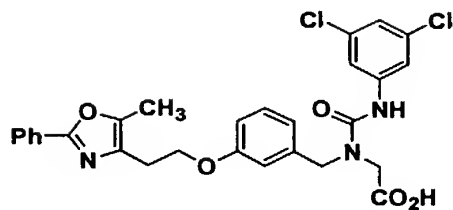
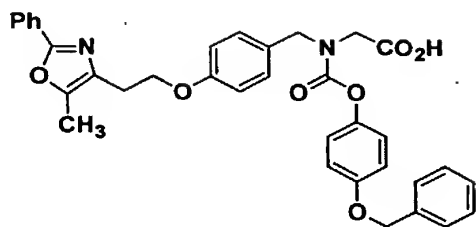
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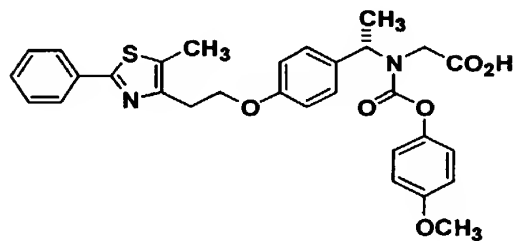
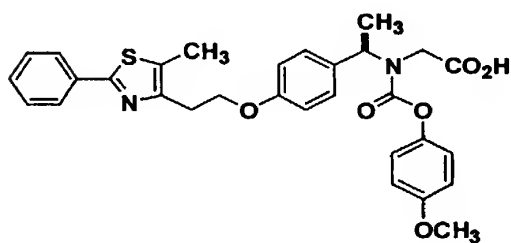
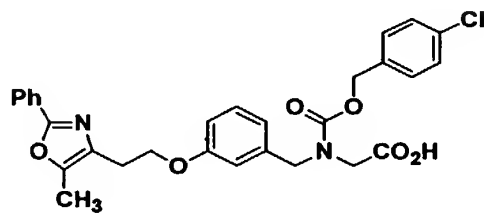
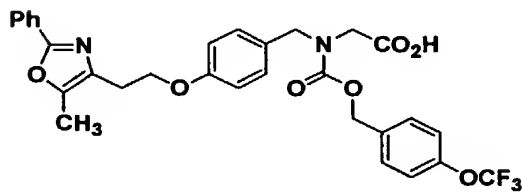
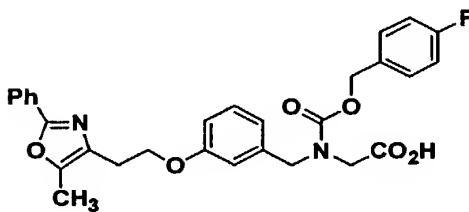
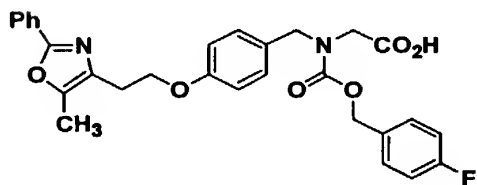
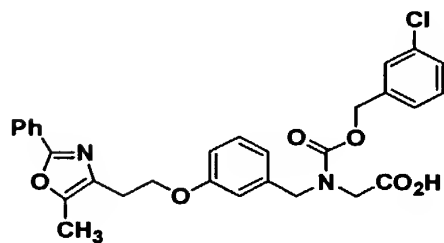
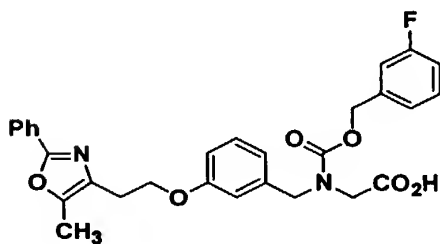
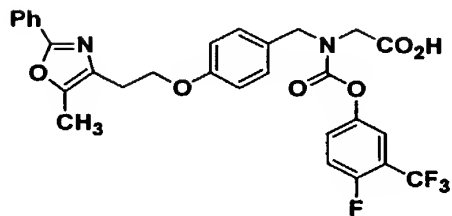
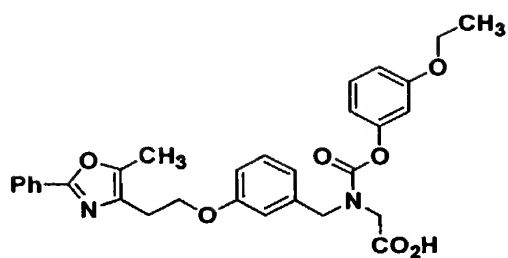
17. The compound as defined in Claim 1 having the structure



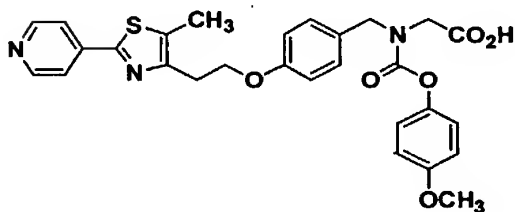




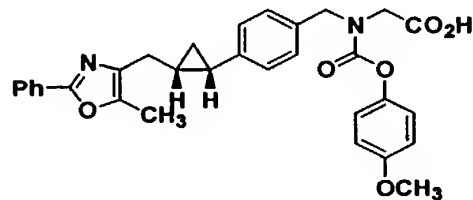
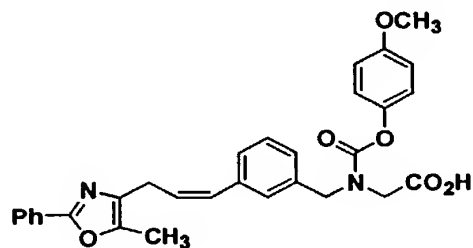
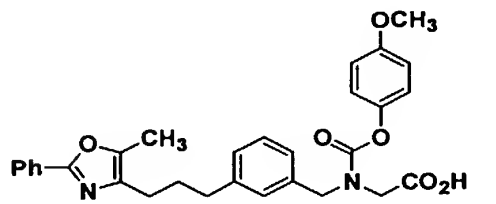
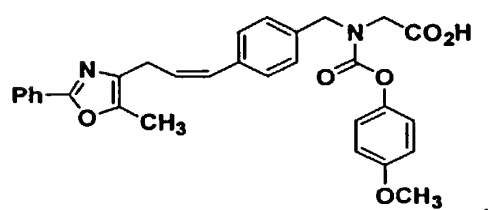
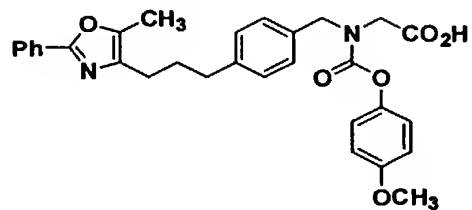




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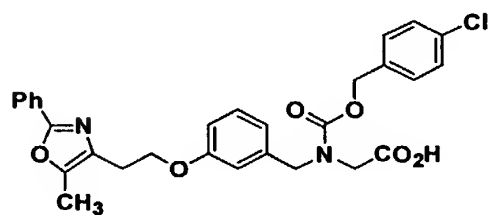
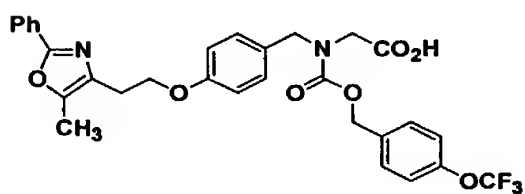
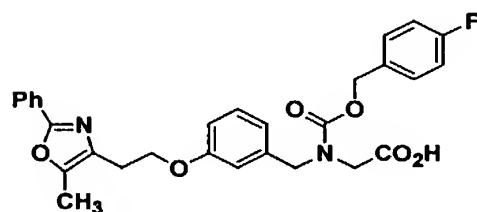
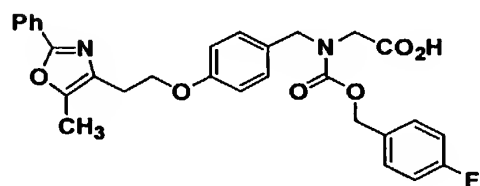
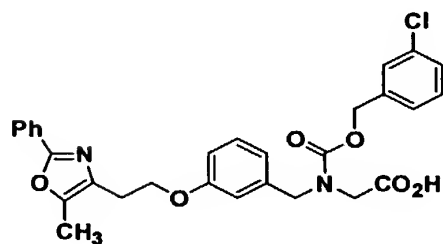
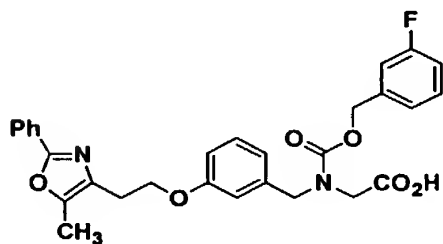
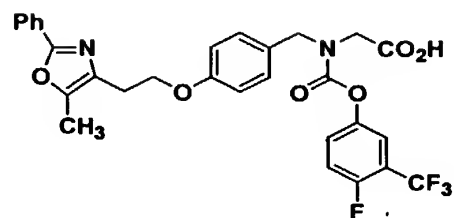
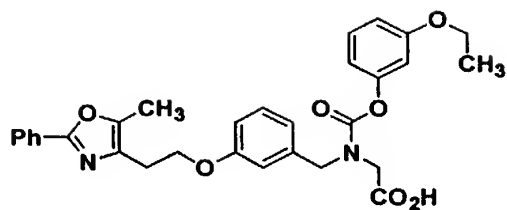
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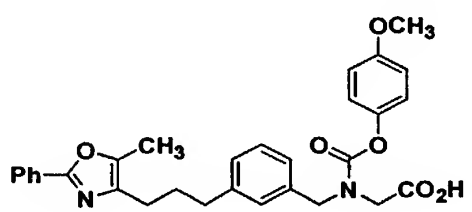
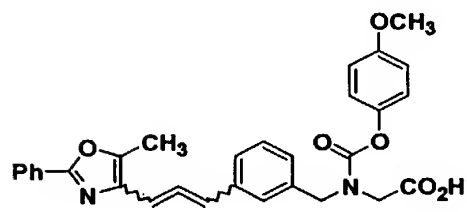
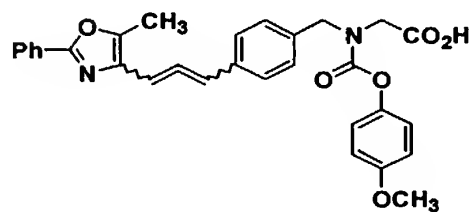
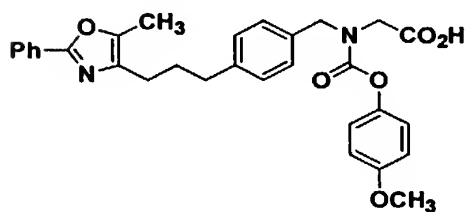
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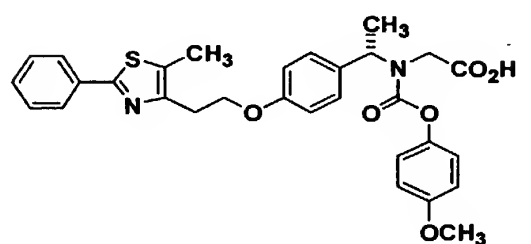
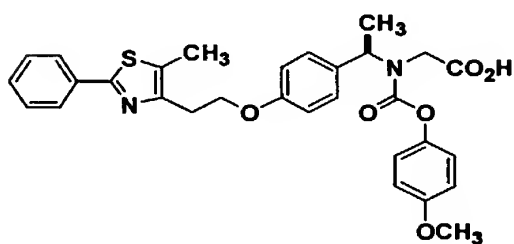
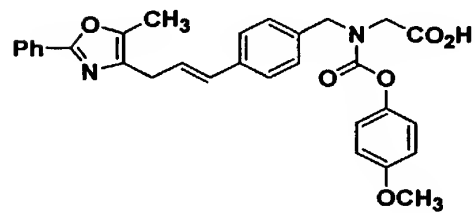
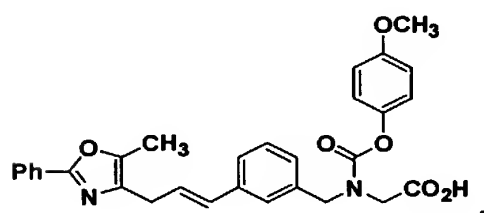
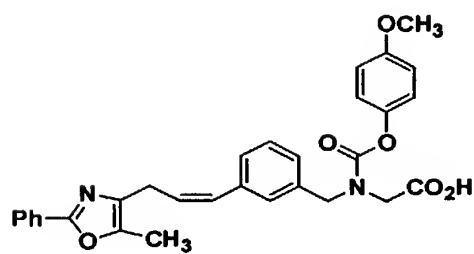
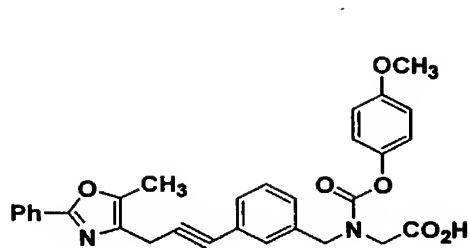


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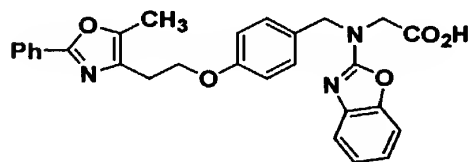
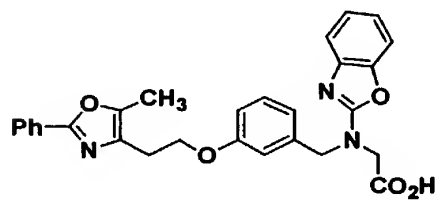
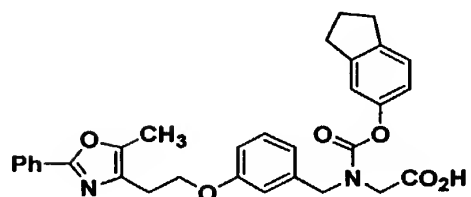
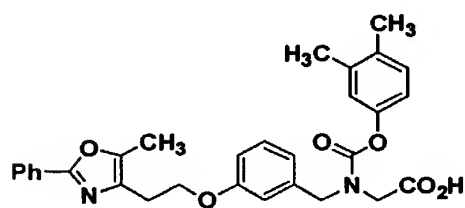
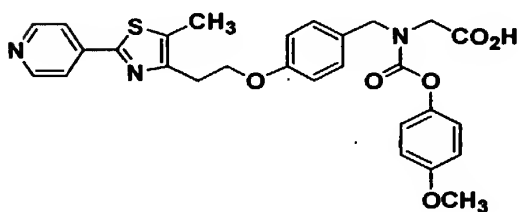


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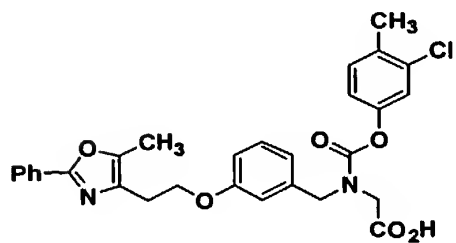
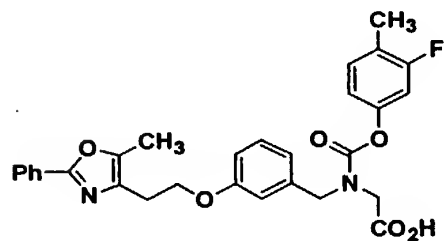
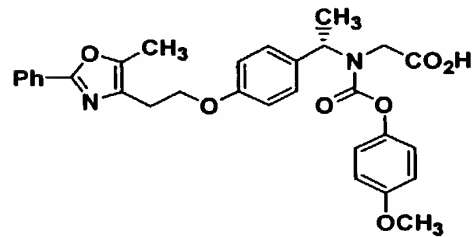
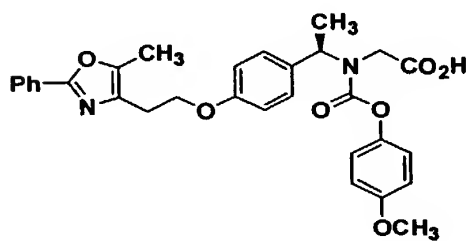
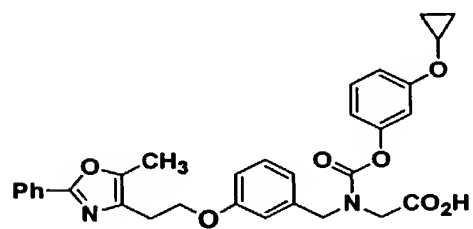
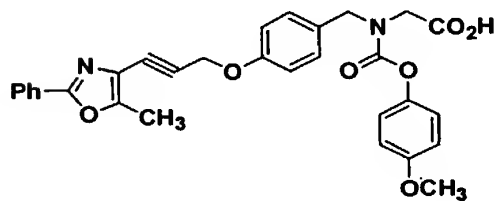
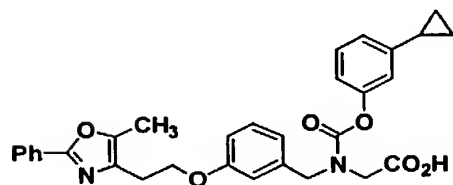
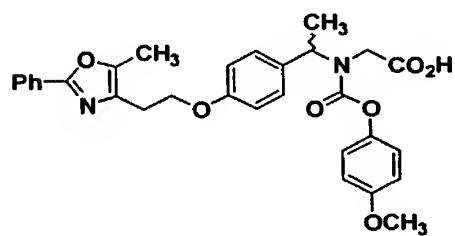
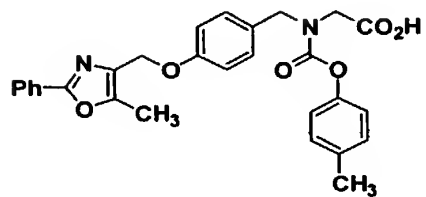


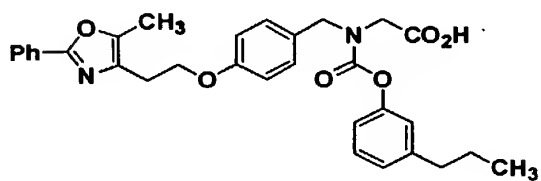
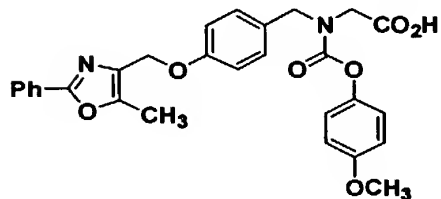
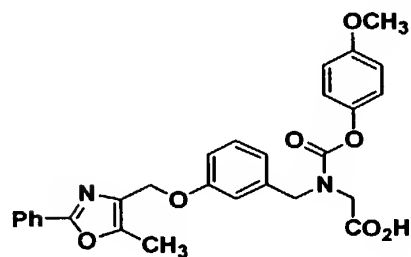
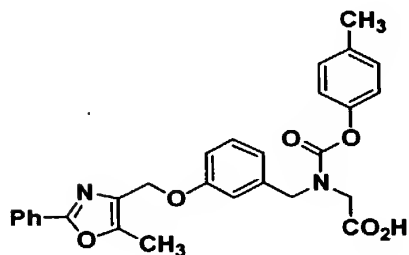
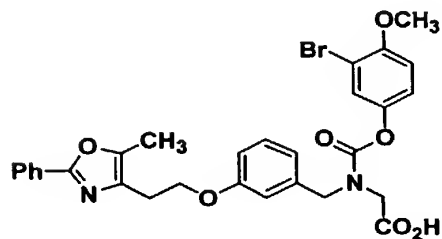
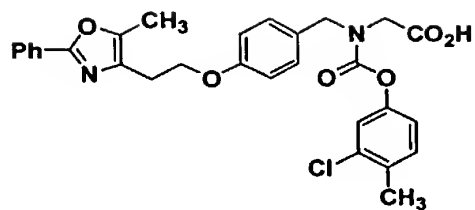


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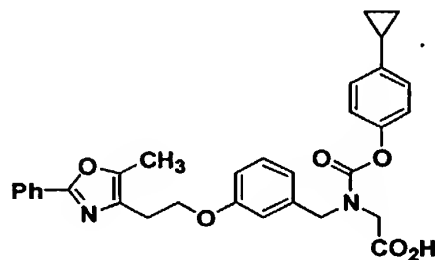
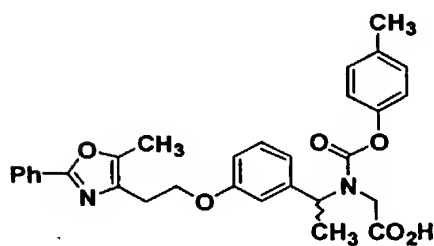
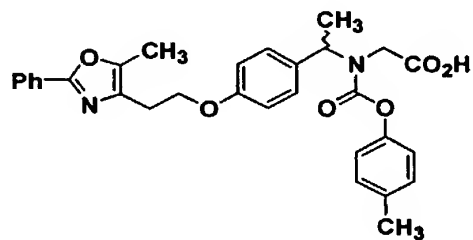
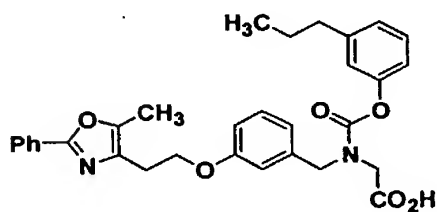


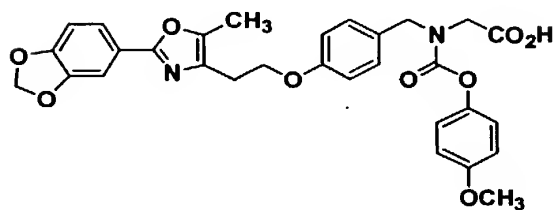
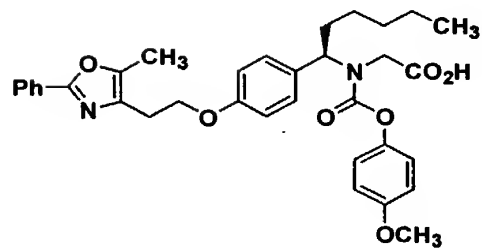
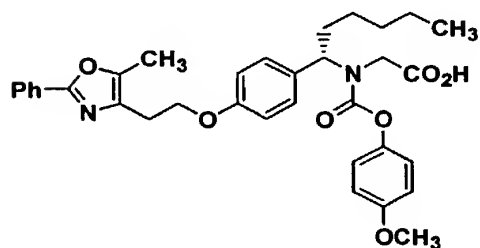
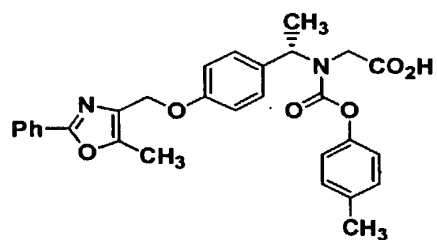
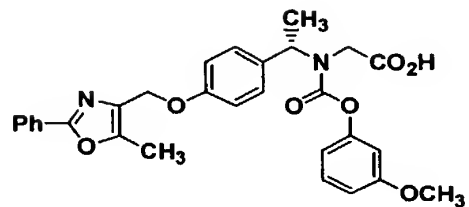
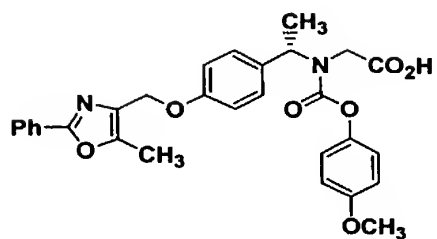
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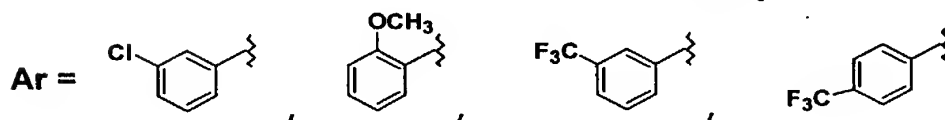
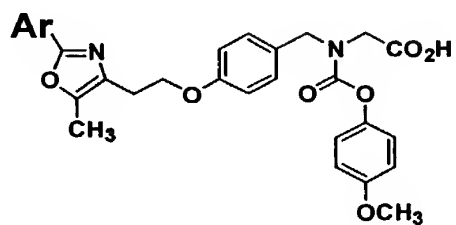


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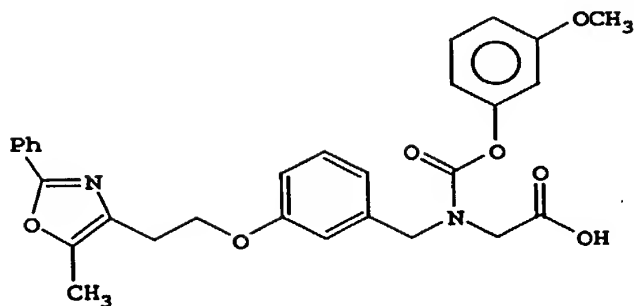
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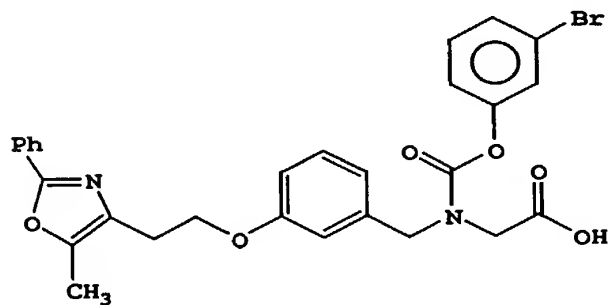
- ## structure



- structure

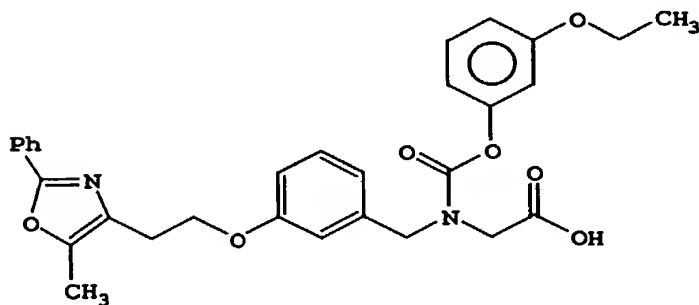


24. The compound as defined in Claim 1 having the structure



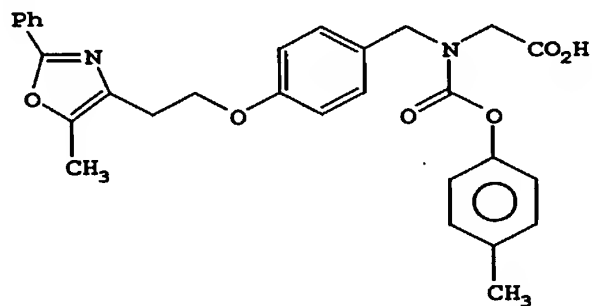
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25. The compound as defined in Claim 1 having the structure

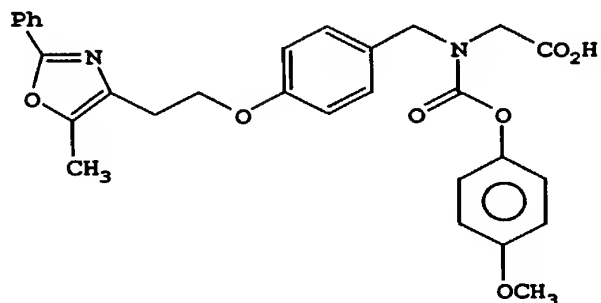


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26. The compound as defined in Claim 1 having the structure

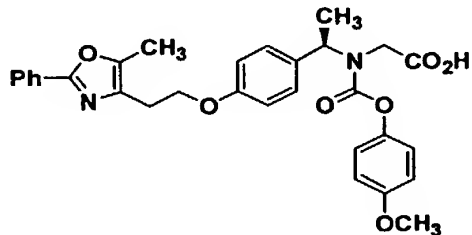


27. The compound as defined in Claim 1 having the structure



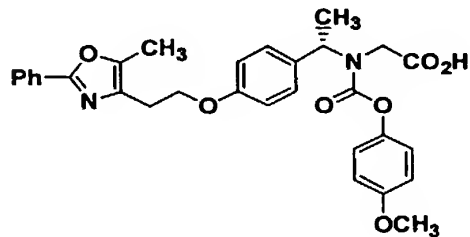
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28. The compound as defined in Claim 1 having the structure

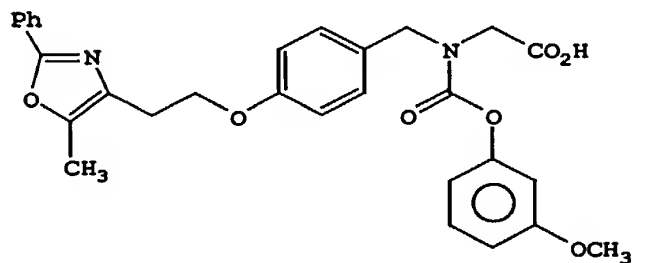


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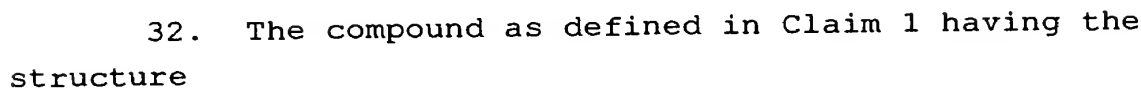
29. The compound as defined in Claim 1 having the structure



30. The compound as defined in Claim 1 having the structure



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33. A pharmaceutical composition comprising a compound as defined in Claim 1 and a pharmaceutically acceptable carrier therefor.

34. A method for lowering blood glucose levels
15 which comprises administering to a patient in need of
treatment a therapeutically effective amount of a
compound as defined in Claim 1.

35. A method for treating diabetes which
20 comprises administering to a patient in need of treatment
a therapeutically effective amount of a compound as
defined in Claim 1.

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37. A pharmaceutical combination comprising a compound as defined in Claim 1 and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

38. The pharmaceutical combination as defined in Claim 37 comprising said compound and an antidiabetic agent.

39. The combination as defined in Claim 38 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR α agonist, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an α P2 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin and/or a meglitinide.

40. The combination as defined in Claim 39 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyrizide, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A.

41. The combination as defined in Claim 38 wherein the compound is present in a weight ratio to the antidiabetic agent within the range from about 0.001 to about 100:1.

42. The combination as defined in Claim 37 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake

inhibitor, a thyroid receptor agonist, an aP2 inhibitor and/or an anorectic agent.

43. The combination as defined in Claim 42 wherein
5 the anti-obesity agent is orlistat, ATL-962, AJ9677,
L750355, CP331648, sibutramine, topiramate, axokine,
dexamphetamine, phentermine, phenylpropanolamine, and/or
mazindol.

10 44. The combination as defined in Claim 37 wherein the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxxygenase inhibitor, or an ACAT inhibitor.

45. The combination as defined in Claim 44 wherein the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, itavastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin and/or LY295427.

46. The combination as defined in Claim 44 wherein
the compound is present in a weight ratio to the lipid-
lowering agent within the range from about 0.001:1 to
about 100:1.

47. The combination as defined in Claim 37 wherein
the antihypertensive agent is an ACE inhibitor,
30 angiotensin II receptor antagonist, NEP/ACE inhibitor,
calcium channel blocker and/or β -adrenergic blocker.

48. The combination as defined in Claim 47 wherein the antihypertensive agent is an ACE inhibitor which is
35 captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril; an NEP/ACE inhibitor which is omapatrilat, [S[(R*,R*)]-hexahydro-6-

an angiotensin II receptor antagonist which is
irbesartan, losartan or valsartan;

49. The combination as defined in Claim 37 wherein
10 the platelet aggregation inhibitor is aspirin,
clopidogrel, ticlopidine, dipyridamole or ifetroban.

51. A method for treating irritable bowel
25 syndrome, Crohn's disease, gastric ulceritis or
osteoporosis, or psoriasis, which comprises
administering to a mammalian species in need of treatment
a therapeutically effective amount of a compound as
defined in Claim 1.

30

52. The method as defined in Claim 36 wherein the disease is a liposarcoma or an epithelial tumor.

53. The method as defined in Claim 52 wherein the
35 epithelial tumor is a tumor of the breast, prostate,
colon, ovaries, stomach or lung.

54. The method as defined in Claim 36 wherein the disease is ductal carcinoma in situ of the breast, lobular carcinoma in situ of the breast, fibroadenoma of the breast, or prostatic intraepithelial neoplasia.

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